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THE SURGICAL CLINICS
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Volume 4 Number 4*

GEORGE W. CRILE AND ROBERT DINSMORE

DEPARTMENT OF GENERAL SURGERY

CARCINOMA OF THE LARYNX

ONE of the greatest triumphs in the history of surgery has been the successful development within the last fifty years of the technic for the complete removal of the larynx for carcinoma, not only with a resultant cure of the disease, but with the satisfaction and comfort of the patient in spite of what would appear to be a hopeless and depressing mutilation. The happy outcome in these cases is strikingly illustrated by the history of 8 patients whom we have seen during the past year, pictures of 3 of whom are given here. All of these were in good health and spirits, with no sign of recurrence, twenty-nine, eighteen, thirteen, ten, four, and three years, and 2 of them one year after operation.

Perhaps no other major operation has had a more immediate popularity than the operation of complete laryngectomy. The possibility of removing the larynx was first demonstrated in the surgical laboratory by Gussenbauer at about the beginning of the last quarter of the eighteenth century. Koeberle in 1856 suggested that a part or the whole of the larynx might be removed with safety. In 1870 Czerny performed laryngectomies

*NOTE.—This number of the Clinics is devoted to various phases of the work of the CLEVELAND CLINIC. This will account for the diversity of its contents, some of the matter being of a medical nature rather than strictly surgical. We are certain that it will be none the less acceptable to our subscribers, who will appreciate the presentation of the various activities of a large clinic.

successfully on dogs. Watson in 1866 performed the first successful laryngectomy in man for a syphilitic stricture, and the first successful laryngectomy for malignant disease was performed by Billroth, whose patient, however, survived for only seven months. The most successful record among the early cases was a case in which a complete laryngectomy was done by Bottini in 1877, the patient being reported as well six years after the operation In 1883, only ten years after Billroth's operation, Solis-Cohen collected records of 65 laryngectomies—4 for non-malignant conditions; 5 for sarcoma, 14 of the remaining 56 being reported as free from recurrence. This is in striking contrast to the record for thyrotomy, which was first done by Brauers in 1833, but forty-five years later, according to Von Bruns, only 19 cases had been reported as having been performed for undoubted malignancy, and of these 19, 2 died from the effects of operation, while of the remaining 17, not one was known to have lived more than a few months As indicated above, this is in striking contrast to the results of laryngectomy secured by surgeons and laryngologists, especially since the development of technical methods whereby the inhalation of blood, wound discharges, and mucus into the lungs, with resultant septic pneumonia, has been prevented We may safely say today that intrinsic carcinoma of the larynx is the most curable of malignant diseases This fact would seem to have been so well established that its reiteration would seem unnecessary were it not for the fact that the query "Surgery or radium?" has recently been extended to intrinsic cancer of the larynx, Pfahler[1] being an apparently ardent advocate of the use of radium in early cases; Quick and Johnson,[2] on the other hand, making the statement: "While treatment of primary operable intrinsic cancer of the larynx is permissible, the evidence to date does not warrant it as the agent of choice"

As, according to Pfahler, the effective method of application of radium includes a preliminary tracheotomy followed by a laryngotomy for the accurate placing of the radium, it would appear that the only possible argument in favor of radium from the point of view of the patient would be the escape from what

is described by some as a hopeless and mortifying mutilation. The photographs published herewith testify to the lack of mutilation, and as for the only disability, the loss of voice, without exception in our experience the patients have acquired an audible whisper which they use without any apparent consciousness of discomfort, either physical or mental, and they are able to swallow, to drink, and to smoke with ease and comfort

Incidence.—Fortunately carcinoma of the larynx is among the carcinomata of least frequent incidence. According to Hoffman's figures the rate of incidence as given in various re-

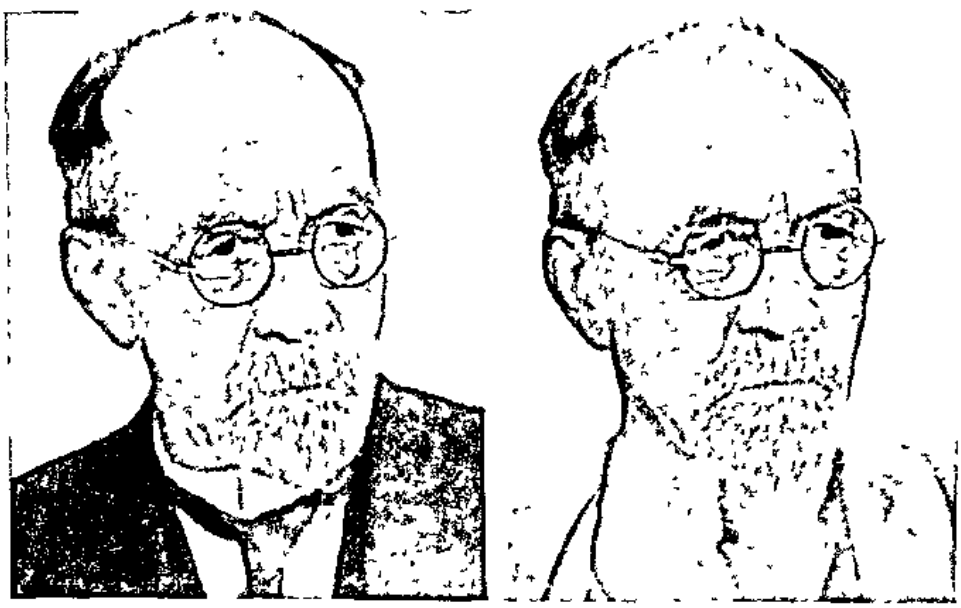

Fig 287.—Patient seventy-two years of age, twenty-nine years after complete laryngectomy for carcinoma.

ports varies from 1.1 to 1.9 per 100,000 males and from 0.1 to 0.5 per 100,000 females. Other tables given by Hoffman[3] show that among malignant growths of all organs carcinoma of the larynx comprises approximately 1.5 per cent. According to Ewing,[4] carcinoma and sarcoma of the larynx comprise from 1 to 5 per cent. of all malignant tumors, and about 16 per cent. of all laryngeal tumors.

The chief age of incidence is the fifth decade. As for the comparative malignancy at the different age periods, it shares with cancer of other parts the characteristic of greater malig-

nancy at earlier ages. There would seem, however, in the case of cancer of the larynx to be a special developmental factor in the production of this age variation in malignancy Thus Sappey has shown that as the network of lymphatic vessels which covers the epiglottis extends toward the arytenoid folds it becomes more and more attenuated until, as it passes from the superior half of the lining membrane of the larynx, it seems to become abruptly impoverished, this attenuation becoming

Fig 288.—Patient ten years after complete laryngectomy for carcinoma

increasingly evident with advancing age This more abundant lymphat c extension might well explain the higher virulence of cancer of the larynx in earlier years

As for the etiology, Jackson[9] claims that from his own experience in 582 cases of proved cancer of the larynx there undoubtedly had been vocal abuse in 376, or 64 6 per cent , this number including public speakers, teachers, singers, hucksters, street hawkers, sales persons, foremen, drill masters, and mechanics and factory employees whose work requires them to

talk loudly in dusty, noisy places. Over- or misuse of the voice is known to cause various laryngeal disturbances which, in turn, become the immediate etiologic factors in the production of carcinoma. Ewing suggests the following lists of etiologic factors: Overuse of the voice, irritant inhalation, sequelæ of exanthems, alcohol, and tobacco.

Treatment.—As has been suggested by the above discussion, and as proved by the end-results, laryngectomy is the operation

Fig. 289.—Patient three years after complete laryngectomy for carcinoma.

of choice in all cases of intrinsic cancer of the larynx at whatever stage of its development. That the operation should be performed in more than one stage, that is, a preliminary tracheotomy, followed at a second séance by the laryngectomy, was early established. We have extended the multiple stage operation in these cases to three stages in addition to the preliminary tracheotomy. The tracheotomy is performed in the usual manner under local anesthesia; the laryngectomy under nitrous-

cancer of the larynx is through the line of esophageal attachment behind and the arytenoids and epiglottis above, particular attention should be paid to the contiguous structures in these directions to make sure that all cancer-bearing tissue is removed. In all cases, but particularly in those in which the growth has extended beyond the larynx in either of the two possible directions, the postoperative use of radium is of value. As would be expected, laryngectomy will usually be followed by a marked local reaction, the extent of which, however, is largely controlled by the preliminary tracheotomy and the fact that the field is left open and lightly packed with iodoform gauze to prevent extension of any possible infection into the mediastinum, final closure being postponed until the reaction and possibility of extension of infection has passed The end of the trachea is freed sufficiently to be brought forward and stitched to the skin, thus assuring protection from the inhalation of wound secretion.

As for the treatment of extrinsic cancer of the larynx, if operative at all, block excision of the cancer-bearing area and of the area of possible extension is essential. In many of these cases surgery, at the best, is but palliative. In many cases a tracheotomy to prevent suffocation is all that the surgeon can offer. Radium for palliation is of special value. It should be borne in mind, however, that extrinsic cancer of the larynx is still more accessible than is cancer of the tonsil or cancer of the pharynx. The striking recovery of the case cited above in which there was a wide extension of the extrinsic cancer should encourage one to attack with faith any but the most certainly hopeless cases.

Among the fatal cases in the personal series of one of us, which includes 36 laryngectomies, in one the carcinoma was entirely extrinsic, the entire esophagus being so involved as to necessitate an esophagectomy in addition to the laryngectomy. In another there were extensive extrinsic involvements which necessitated the removal not only of the larynx but also of the epiglottis, part of the esophagus, the hyoid, and block dissection of the glands on the right side of the neck with the sternomastoid muscle. In another the patient had received prelimi-

nary treatment with radium and the laryngectomy was an operation of last resort

The postoperative care of these patients is of the highest importance, in fact, there is no condition that requires more careful and constant postoperative nursing observation. We have always felt that the finest individual examples of nursing care that we have seen have been in this group of patients The prevention of pulmonary complications means that not one drop of blood, of mucus, or of wound secretion shall be aspirated into the trachea, it is therefore necessary for the nurse to be constantly at the bedside of the patient The possibility of pulmonary complications is greatly lessened if the tracheotomy tube is removed early, thus leaving the trachea free from the irritation of the tube, as this tends to cause tracheitis, with occasional resultant pneumonia As the granulations close in around the trachea the need for constant care is greatly lessened The packing in the neck is changed frequently and the wound surfaces are kept absolutely clean and dry An occasional dichloramin-T dressing is substituted for the plain gauze packing

The use of the duodenal tube for feeding solves one of the especially troublesome postoperative problems—the loss of weight and strength as the result of dysphagia By the use of the duodenal tube we have sometimes given these patients as much as 10,000 calories each twenty-four hours, the nurse literally pouring food into them at frequent intervals All forms of gruels mixed with syrups can be used for these high caloric feedings, but patients do not tolerate these as well as they do the pure vegetable gruels By grinding them very finely nearly all the vegetables can be utilized, and it is surprising how large an amount of vegetables and of meats can be thus given It is advisable if possible to insert the tube for a day or so prior to the preliminary operation, and to keep the tube *in situ* until after the plastic operations have been done

Frequently these patients suddenly develop a marked dyspnea and cyanosis as the result of the formation of plugs of mucus low down in the trachea These are usually expelled by coughing Occasionally this is impossible and the plug must be

dislodged. For this purpose the nurse should always have at hand an ordinary No. 32 catheter. As soon as the plug is loosened it can be quickly expelled by coughing

Summary.—In brief recapitulation, then, we may summarize our point of view as to cancer of the larynx as follows:

1. Intrinsic cancer of the larynx is completely curable by laryngectomy.

2. Cancer of the larynx which is both intrinsic and extrinsic may in certain cases be completely cured by laryngectomy and a wide excision of the cancer-bearing area.

3. The postoperative application of radium or of the *x*-ray is of value

4 Frequently in inoperable cases of extrinsic cancer of the larynx only tracheotomy and the palliative use of radium are indicated.

5. Operation for extrinsic cancer of the larynx should always include block dissection of the indicated gland-bearing areas

6. Local anesthesia alone or, better, combined with nitrous-oxid-oxygen is the anesthetic method of choice.

7. Multiple stage operation in three stages in addition to the tracheotomy is required to assure the minimum reaction and the maximum freedom from postoperative complications.

8. The postoperative care of these patients is of the utmost importance and should be in the hands of especially instructed nurses and under the constant supervision of the surgeon

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GEORGE W. CRILE

DEPARTMENT OF GENERAL SURGERY

THE FACTORS THAT GOVERN THE SURGICAL MORTALITY OF OPERATIONS FOR HYPERTHYROIDISM

SINCE it has always been our policy to operate upon all patients with hyperthyroidism except those in delirium, it is possible to trace the successive steps in the evolution of our present plan of management, whereby one by one the factors of special menace in these cases have been attacked and conquered.

EVOLUTION OF PLAN OF MANAGEMENT

1. At first the patients were taken to the operating room on a previously determined date. The family and friends were thus given ample opportunity to express their well-grounded forebodings and fears by a protracted awe-inspiring séance of abortive attempts to cheer the patient with trembling lips and moist eyes and to bid him farewell, only too often a final farewell. Ether anesthesia was administered by the intern anesthetist and a strictly anatomic excision was made by a cadaveric technic. The operative mortality was 16 per cent. and deserved to be higher.

On one day a patient, thus ominously prepared, arrived in the anesthetizing room in tumultuous delirium, singing gay college songs and requiring the application of the barbarous methods of restraint then employed as he passed through the "excitement" stage of ether anesthesia. This patient never regained consciousness and died that evening with a temperature of 110° F.

2. This tragic case led me to the obvious conclusion that no patient should be anesthetized when in such a state of great ex-

citement. A few days later a young woman was brought to the anesthetizing room in a state of overwhelming excitation, though she was not actually delirious She was promptly sent back to her room without any attempt being made to anesthetize her Nevertheless, this patient also rapidly became delirious and died that night with a temperature of 109° F.

3 As the result of these experiences a prolonged research was undertaken in which the effects of fear on the bodily processes of animals were studied The findings in this research have been published in the papers included in the book entitled, "The Origin and Nature of the Emotions" The tragic deaths of these patients were not in vain, for they led to the elimination of the last parting scenes in the patient's room, of the dramatic journey to meet the unknown in the operating room; of the anticipation of the fateful day and hour; and of the knowledge that an anesthetic was being administered The difficult task of keeping the patient in ignorance of the administration of the anesthetic was entrusted to Miss Hodgins, who established a routine whereby the patient was successfully anesthetized after several days of fictitious "anesthesia" by means of inhalations of various agents

As the result of this change in the method of administering the anesthetic the operative mortality fell materially, but we found that the pulse-rate ran up during the operation, and on close analysis we found that this increased pulse-rate was related as clearly to the injury of operation as the effect of hitting the thumb of a conscious person with a hammer

4 This clinical observation was easily confirmed in a research on animals which showed that ether anesthesia protected the animal or the patient from the conscious appreciation of the bodily injury, but not from its effects, that ether anesthesia was only a veneer, the patient responding to injury as he would respond without anesthesia, that in effect the patient was crying under the surgeon's every blow; that, bereft of his power of speech, he was mutely expressing his pain to the surgeon by the tumultuous heart, the rapid pulse, the heavy respiration, by sweating, by tremors, by the immediate hyperchromatism and

succeeding chromatolysis of the cells of his brain and liver and adrenals—that is, by all the organs of his body the patient was mutely appealing for mercy, his widely dilated pupils in vain beseeching the surgeon to cease his cruel work.

This research and these clinical observations divorced dissecting-room methods from the operating room by granting to the anesthetized patient the rights of the conscious.

By flooding the field of operation with a local anesthetic and eliminating rough handling of the tissues the biologic protests of the organism were eliminated.

5. Again our results were much improved, and now at last we thought we had conquered the field, only to find that as we eliminated the outstanding causes of the tragic sequelæ of our earlier cases, a new and unsuspected danger was revealed, namely, the inhalation anesthetic. In our bad risk cases we sometimes found that when they reached the operating room they were in a state of nausea which was not readily overcome by deeper anesthesia as in ordinary cases, the condition resembling the acute abdominal cases *in extremis*. Consequently, after a death had followed operation in such a case in which continuous vomiting and progressive mounting of all the symptoms continued until death, we decided not to operate in the presence of persistent nausea; just as we formerly decided to omit operation in the presence of acute fear.

One day an emaciated patient was anesthetized in her room and brought to the operating room, but because of persistent nausea no operation was performed, and the patient was returned to her room under anesthesia. Nevertheless, this patient died—the vomiting never ceased until death, the temperature ran up to 108° F., the pulse to 210, delirium developed, and death closed the story. It was obvious that the indirect cause of death was the ether anesthesia.

6. This problem, in turn, was promptly taken to the laboratory, where Dr. M. L. Menton and I found that not only ether and chloroform, but all inhalation anesthetics cause acidosis; that the hydrogen-ion concentration of the blood progressively increased with the depth of the anesthesia, death occurring at

the moment when the boundary line between alkalinity and acidity was reached. We learned that living processes can continue only in a neutral or alkaline medium and that inhalation anesthesia drew life against the deadline. Since the effects of the lipoid anesthetics persisted beyond the completion of the operation, they were by so much the more deadly. This finding disqualified ether or chloroform as the anesthetic in any serious risk. We found, on the other hand, that while full general anesthesia with nitrous oxid also produces acidosis, the acidosis disappears almost instantly after the administration of the anesthetic is discontinued Because of this fact, and for other reasons that need not be entered into here, nitrous-oxid-oxygen became the anesthetic of choice The working out of the difficult technic for the successful administration of nitrous-oxid-oxygen was entrusted to Miss Hodgins, whose mastery is indicated by the fact that 51,000 white patients have been anesthetized by Miss Hodgins and her trained anesthetists without a death

We still found, however, that in certain cases the acidosis from the protracted anesthesia even with nitrous-oxid-oxygen was sufficient to cause death

7 If a very sick patient cannot be taken with safety to the operating room without anesthesia and if the protraction of the anesthesia caused by its administration in the patient's room carried the patient across the deadline, then the operation must either be declined or else performed in the patient's room under local anesthesia and the lightest possible nitrous-oxid-oxygen anesthesia We therefore turned our operating-room conceptions topsy turvy, and since the patient could not be taken to the operating room, we took the operating room to the patient Moreover, we took a cue from our dental colleagues and developed for general surgery analgesia, which is that ephemeral misty stage of anesthesia in which the patient is bereft of all fear, worry, and anxiety, and of from about 60 to 80 per cent of the pain

Our plan of management was soon so developed that ligations and thyroidectomies could be easily done without moving the patient from his bed. Asepsis was just as complete as in

the operating room, and we thought that at last this rough unhappy road had terminated in a smooth road free from danger Certainly our control of the very bad risk cases had been greatly improved. But we found that this last tactical step revealed still another hurdle, for in a small number of cases there was still a violent reaction. This could not be due to fear, as there was none. It could not be due to trauma, for the field of operation was completely blocked with novocain, and the reaction did not appear during or just after the operation. The reaction could not be due to the anesthetic, for there was no full anesthesia. Occasionally we could overcome this violent reaction by complete refrigeration, but we could not feel content, or indeed safe, with less than its prevention. What could be this x factor?

8. By comparing this clinical observation with the sequelæ of operations in other regions we noted that there is usually a postoperative increase in temperature during the first and second postoperative days which is independent of infection. This increased temperature, in part at least, is due to the absorption of aseptic wound secretion. Now a patient with hyperthyroidism is hypersensitized to every stimulant—to fear, to injury, to thyroid extract, to iodin, to adrenalin, to toxins, to infections. Why would he not be hypersensitized to the aseptic wound secretions as well? If, then, a patient were hypersensitized to a degree, let us say five times that of the ordinary case, it would follow that an amount of aseptic wound secretion that in an ordinary case would raise the temperature one degree would raise the temperature of the fivefold hypersensitized patient 5 degrees; of the tenfold, 10 degrees, etc.

The obvious test of this assumption was to leave the wound wide open, dressing it with flavine gauze or with plain gauze, so that the secretion would be absorbed by the gauze and not by the raw wound

This proved the case, and we found that when the wound was left open for four, eight, twelve, or twenty-four hours, the increase of temperature from the absorption of wound secretion was eliminated.

9. By this time the mortality had fallen from about 16 to about 1 2 per cent.; but there was still left the desperate case which we still occasionally lost—that is, the patient who is reduced to skin and bone, weighing from 70 to 90 pounds, with a hopelessly broken compensation of the myocardium, with swollen extremities, perhaps with ascites, in whom the superior thyroid artery beats under the loose skin with a rhythm which can be seen across the room. In such a case life is balanced on a slack rope. The most inconsequential touch will terminate it. Even if we could wish out the circulation of the superior thyroid artery, the patient might die as the result of the metabolic disturbance from the weakened circulation.

It was obvious that in such an emergency some entirely different type of procedure was needed than in the conditions already met and conquered. Heretofore we had been subtracting from the patient the evils brought by ourselves, and had been leaving the resources of the patient as they were—*i e*, neither reduced nor augmented The elimination of fear, of the trauma, of the inhalation anesthetic, of the wound secretion, the operation on an undisturbed pillow, the elimination of disastrous waiting—all these were subtractions by the surgeon of evils brought by himself. What can the surgeon add for the reinforcement of the weakened defenses of the patient? What should be the crucial point of attack. The crucial point is the utter feebleness of the internal respiration in the cells of the essential organs, notably the myocardium, the brain, the liver The circulation is so feeble in the capillaries, the acid waste products from the furious metabolism form so rapidly in the cells, the organism so rapidly loses water by vomiting and sweating; and the intake of water is so much diminished that the living processes in the cells themselves are failing What can be done?

The essential procedures are: (1) To digitalize the failing heart muscle so as to promote the minute circulation of blood in the tissues, (2) to flood the desiccated organism with water by hypodermoclysis; (3) to increase the blood volume and, hence, the capillary circulation by blood transfusion; (4) to diminish the metabolism by all the intriguing care of a comprehending

"never-say-die" nurse, by encouragement, by sleep and rest, induced when necessary by sedatives or opiates. Thus, by calming the patient; by building up the tone of the myocardium, the brain, and the liver; by a "touch-and-go" ligation on one side only, the patient may be tided over the most critical period.

Sometimes, especially if the patient is a woman, she may be sent home for a time and then return for the second ligation. Thus, on the one hand, by preserving the reserves which the patient still has, and, on the other hand, by supplementing the failing resources of the patient, we have been able to save these derelicts, with the exception of but one type of case, fortunately very rarely encountered, namely, the delirious patient.

As the result of the adapted application of the plan of management the evolution of which we have described, we are now able to seize and hold the initiative and to undertake operation upon every patient except those who are delirious. As these patients have undergone no great hardship, have little or no knowledge of their operation, have not seen either surgeon or operating room on the day of operation, other patients come free from fear and anxiety, so that the community as well as the patient becomes anociated.

GEORGE W. CRILE AND ROBERT DINSMORE

DEPARTMENT OF GENERAL SURGERY

DIVERTICULA OF THE ESOPHAGUS

IN view of the various discussions of diverticula of the esophagus which have recently appeared in the literature, in particular the important articles by C H. Mayo,[4] Lahey,[3] and Bevan,[1] a short review of our cases may be of interest

The average age of our patients has been fifty-six years; the youngest being a male of thirty-eight years and the eldest a male of seventy-two years. The preponderance of males in our series has been in accordance with the ratio cited by Lahey—about 4 to 1

The two most common symptoms presented by our patients have been difficulty in swallowing and regurgitation According to the histories of these cases, the difficulty in swallowing has usually become progressively worse until in some cases the patient was able to swallow only liquids. The regurgitation has been either of mucus or food; one patient described it as "sour mucus or slime." One patient developed what she described as a "squash sound," which was due, as Lahey has indicated, to a mixture of air and food within the sac. Many other symptoms have been presented which were dependent for the most part upon the size, shape, and position of the diverticulum.

The diverticula in all of our cases have been globular in shape and apparently of the true pulsion type, none of them having justified the diagnosis of a true traction or Rokitansky diverticulum. In one patient the diverticulum, an *x*-ray of which is shown (Fig. 290), was associated with a marked cardiospasm. It was found later that this patient had also a carcinoma of the esophagus.

The only effective treatment for these cases is the removal of the diverticulum by an external operation which should be done in two stages, as was first suggested by Goldmann of Freiburg (1909), the operation being later modified by Murphy. Murphy, however, did not perform the second operation—the

Fig. 291.—Esophageal diverticulum—carcinoma. Male, fifty-eight years of age; duration of symptoms two years; irritation in throat; for six weeks unable to swallow or use voice; inoperable carcinoma directly beneath diverticulum.

excision of the sac—until the fourteenth day after the primary operation. We have found that this length of time is not necessary, and do the second operation four days after the primary procedure.

We use a transverse incision made in the natural fold of the neck, similar to a thyroidectomy incision, rather than the in-

cision commonly adopted, which is made anterior to the sterno-cleidomastoid muscle. We feel that the transverse incision results in a less conspicuous scar, while just as good an exposure is secured as by the other method. After the thyroid has been

Fig 292.—Esophageal diverticulum. Male, fifty-three years of age, duration of symptoms three to four years, difficulty in swallowing, interference with respiration, especially when lying down, cough and mucus, two-stage operation, complete cure

freed from its capsule, it is lifted up and drawn forward, the diverticulum then being dissected out and iodoform gauze packed around it. Ninety-six hours later the neck of the sac is excised and the opening closed with either a purse-string or a

mattress-suture, which completely covers the opening. In 1 or 2 cases the walls of the sac were found to be extremely thin, and in the process of dissection it inadvertently was opened. When this occurs, and, in consequence, it becomes necessary to excise the sac at the time of the primary operation, the wound is packed open and a secondary closure is made four days later.

Fig 293 —Esophageal diverticulum Male, fifty-seven years of age, duration of symptoms two years "Food sticks in throat and again lower down in chest." At times coughs up food; two-stage operation, complete cure

As after laryngectomy, the postoperative care of these patients has been greatly simplified by the use of the duodenal tube, which should be inserted prior to the operation if the patient is able to swallow. If not, it can readily be inserted at the time of the operation However, it should be in place before any plastic work is done on the esophagus.

Jackson has advocated a very ingenious method for localizing the sac during the operation. He inserts a small endoscope into the sac, the resultant illumination from within guiding the surgeon in the dissection. In most cases, however, there is little difficulty in locating the sac

Fig 294.—Esophageal diverticulum. Male, sixty-five years of age; duration of symptoms ten years, cough worse at night, large expectorations; for last three to four years increasing difficulty in swallowing; can swallow only liquids, loss of 20 pounds in weight, two-stage operation; complete cure

The adoption of the two-stage operation for the removal of esophageal diverticula has practically reduced the mortality to zero, since the fatal mediastinitis which often followed the one-stage operation is prevented. In our series of 10 operative cases there has been no death.

Fig. 295.—Esophageal diverticulum—large multiple adenomata Male, fifty-two years of age, duration of symptoms three years; difficulty in swallowing; regurgitation of food two to three hours after meals; thyroidectomy and excision of diverticulum; cured.

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FRANK E. BUNTS

DEPARTMENT OF GENERAL SURGERY

A CLINICAL DISCUSSION OF TUMORS OF THE BREAST

THE problems presented to the surgeon by the presence of abnormal conditions of the breast, as by those of the uterus in the child-bearing period, cannot as readily be solved as can those presented by similar conditions in other organs or tissues. In other organs and tissues a possibly precancerous lesion, if accessible, is removed without question, and in doubtful cases the excision may be extended to include the adjacent tissues so as to block the avenues of local and metastatic extension.

In the case of the breast, on the other hand, a radical operation must include the entire breast, with the chain of lymphatics to and in the axilla, and no woman consents readily to such a mutilating operation, especially in the prime of life; and even though her intelligent comprehension of the possibility of cancer development and extension may lead her to an apparently willing consent, the resultant mortification, even though silently borne, is no light matter.

There can be no difference of opinion as to the fundamental procedure once a diagnosis of malignancy has been definitely established. That any benign growth should be removed is as certain. The problem is to decide what conditions are potentially precancerous, and if precancerous, whether a policy of watchful waiting is permissible, or whether radical removal of the entire gland-bearing area should be performed at once. It is particularly essential that the general practitioner be convinced regarding these problems, for it is to him that the patient first presents herself, and it is upon his encouragement and advice that she will depend for guidance as to the validity of the dictum of the consulting surgeon; it is under his eye that

a period of watchful waiting must be passed if in any case such a period is deemed advisable; his must be the final decision as to when the patient shall return to the surgeon for further operation.

While the cause of cancer is not known, that certain conditions, such as trauma or continued irritation, for example, definitely predispose to or excite the development of cancer, is generally conceded. Among the so-called benign breast lesions which should be examined as to their possibly precancerous character are diffuse hypertrophy, traumata from blows or continued irritations, chronic mastitis, cysts, and the so-called benign tumors. The relation of the precancerous potentiality to lactation is also of importance.

In Hoffman's statistical studies of cancer[1] an analysis of 314 fatal cases of cancer of the breast showed as the probable exciting cause "trauma, 44; childbirth, 13; mastitis, 7; tumor of breast, 5, abscess of breast, 2, ulcerated nipple, 1; fissure of breast, 1 " In the combined experience of my associates and myself in 695 cases of carcinoma of the breast there was an antecedent traumatic history in 93, 13.4 per cent ; 12 cases had had the breast massaged, and 39 had a history of abscess or "caked breast "

While the relation of the location of a cancer in the breast itself may not give a clue as to the etiologic factors involved, we have been interested to find in a study of 180 cases in which the location was cited that 47 per cent were located in the upper outer quadrant (Fig 296)

The possible relation of carcinoma to lactation is suggested by the fact that our figures indicate that approximately 90 per cent. of the cases of carcinoma in women had lactated. That a functioning breast has some value as a causative factor is suggested also by the fact that among the 25 cases of tumors of the breast in men in our series only 3, 12 per cent , were cases of carcinoma, as opposed to an incidence of carcinoma among the cases of breast tumors in women of 55.8 per cent This important point needs to be checked by more careful inquiries as to the history of lactation in each case

Trauma.—Whatever may be the developmental process within the cells which changes normal tissue into cancerous tissue, and however difficult it may be to explain how that process can be initiated by a traumatism, a definite relation between trauma of the breast and the development of cancer is certainly

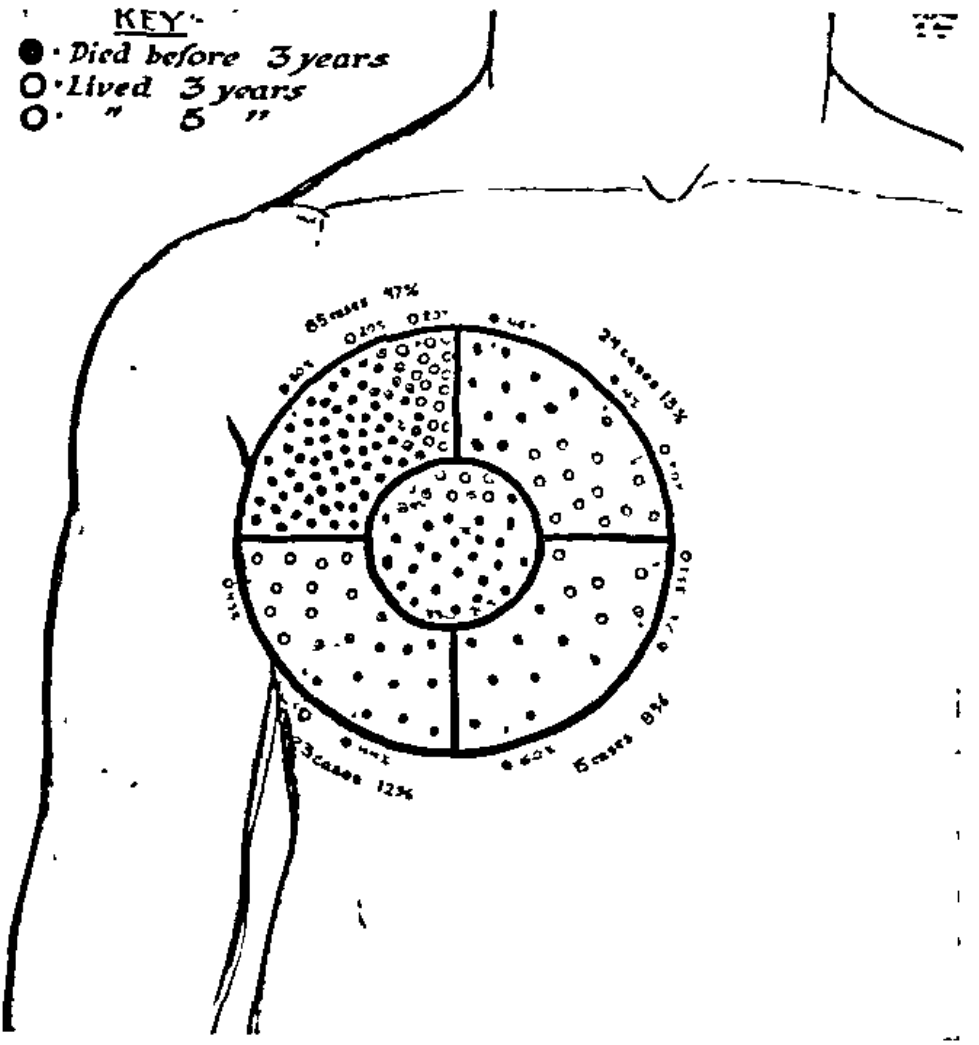

Fig. 296 —An analysis of the location and end-results of 180 cases of carcinoma of the breast.

indicated by such figures as those in our own series and those cited by Hoffman.

I recently performed a radical amputation of the breast in the case of a woman who only three months before had suffered a severe blow on the chest. A small hard lump developed almost immediately on the upper outer quadrant of the right breast, which at operation was found to be a carcinoma, though

not larger than an acorn As there was no previous history of any abnormality, and the appearance of this growth immediately followed the injury, it is difficult to see how the latter can fail to be the immediate contributing cause of the carcinoma

In any case the association of trauma and carcinoma is sufficiently indicated to warn the physician who may be consulted after such an accident that frequent painstaking examinations are essential; and that while the patient should not be unduly alarmed, the importance of repeated examinations should be emphasized.

In this connection the dangers of breast massage may be mentioned Any but the gentlest manipulations may be sufficient to induce in the soft non-resistant tissues of the breast a definitely precancerous traumatic lesion, while once the carcinomatous invasion has been initiated, massage will promote the dissemination of metastases Dr Knox, of the Institute of Cancer Research of Columbia University,[2] has shown that "very gentle massage for a total period of from two to five minutes distributed over a number of days has set free numerous particles of tumor which form emboli in the lungs." So far as my own experience has gone, every case of cancer en cuirasse has been preceded by massage Dr Knox says further, "The effect of pressure, rubbing, or active massage on the tumor has been frequently observed in human beings as the result of osteopathic or massage treatment of malignant tumors and many examples have been seen in recent years of wide dissemination of a primary growth very effectively accomplished by this procedure

"Such an instance has recently occurred at St Luke's Hospital, and furnished one of the rare instances in which extensive gross metastatic invasion of muscle could be observed The patient stated that massage treatment had been regularly employed for some time previous to admission When the breast tumor was examined there was found a fairly extensive area of eczema overlying a large very hard tumor which was fixed to the pectoralis fascia Small white tumor nodules were scattered widely throughout the muscles, even invading the individual fibers"

In our own series, as stated above, 12 cases gave a history of massage of the breast. It would appear that in the treatment of any abnormal condition of the breast massage should rarely, if ever, be applied—at least, until our knowledge of the factors which may predispose to, or may be the direct cause of, cancer is much farther advanced than it is today.

Hypertrophy.—True hypertrophy of the breast is always pathologic. Occasionally in a young unmarried woman there occurs a symmetric diffuse enlargement of both breasts—the so-called virginal hypertrophy—which is seldom suspicious. but in

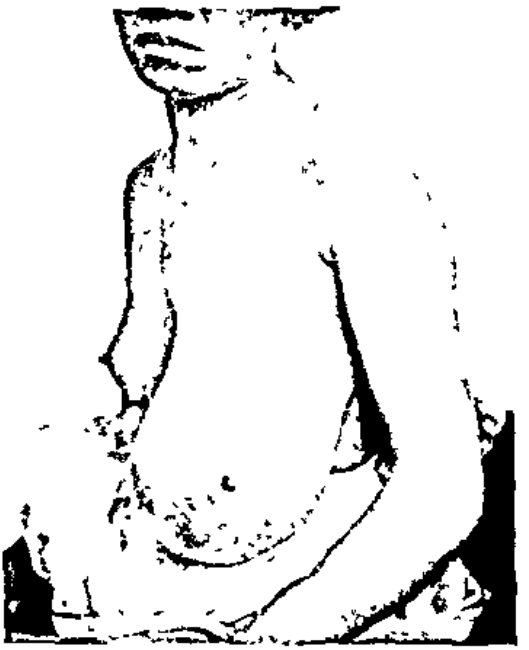

Fig 297.—Hypertrophy of the breast in unmarried woman aged twenty-eight.

rare instances the occurrence of carcinoma has been associated with this type of enlargement. Here again there may be no direct relation between the two conditions, but nevertheless, since the hypertrophy is an abnormal condition, especial watchfulness for the development of a localized lump is indicated (Fig. 297).

Another type of hypertrophy which Bloodgood designates "senile parenchymatous hypertrophy" is a change which begins during or after the menopause. It may throughout partake of the character of benign cysts, or be of an adenocystic type (Bloodgood) with carcinoma as the frequent sequel. While because of its cystic nature this lesion is more properly dis-

cussed in the following section, it is mentioned here to emphasize the prime importance of immediate exploration, with removal of the entire breast if the lesion is of the precancerous type.

Cysts: Cystic Mastitis.—The difficulty of forming any generalized conclusion regarding the relation of cysts to cancer is indicated by Deaver's[3] grouping of breasts which had been removed because they were supposed to be precancerous or in an incipient stage of cancer. Fourteen types of tissue were found ranging from normal to frank cancer, and among these fourteen, ten contained cysts. In these ten groups the cysts varied from

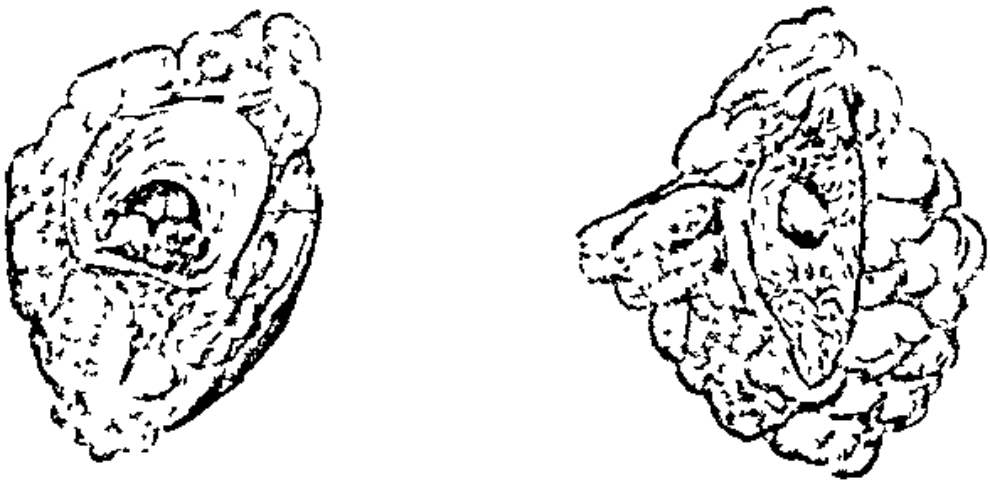

Fig 298.—Papillomatous cyst of breast. The patient from whom this specimen was removed had had several attacks of pain and swelling in the left breast. It was impossible to determine preoperatively whether the condition was cancer or chronic mastitis. The pathologic report was chronic cystic mastitis with tendency to cyst formation.

a closely approximated group of pin-head size to large nodules; the contents of the cysts and the character of their walls varied, in some the external appearance seemed normal; in others the presence of the cyst was evidenced by a firm, well-circumscribed mass. As this is a clinical discussion, I do not propose to list any of the classifications which have been based upon the histologic structure, but rather to consider in the face of this diversity of character what shall be our procedure (1) in cases in which the presence of one or more well-localized cysts is clearly demonstrable, and (2) in cases in which an apparent hypertrophy, or a general lumpy texture, suggests a more general cystic condition.

That a single cyst should always be removed is, in my opinion, unquestionable. Whether or not the full breast should be removed is not a settled question. It would seem that in the case of a single cyst which histologic examination proves to be benign its excision is sufficient, provided that both breasts are examined at stated intervals to assure the early discovery of the enlargement of any cyst which may have escaped the primary examination.

In the cases of so-called abnormal involution or chronic cystic mastitis it appears to be the opinion of most surgeons that this is a possible precancerous condition. Therefore, when a breast has a general dense feeling or is generally "lumpy," an exploratory incision is advocated with a radical operation if carcinoma is present, removal of the breast if there are areas of doubtful character, and in certainly benign cases only the removal of the cystic area or areas (Fig. 298).

We cannot agree with Deaver[4] in his analysis of the results of 83 cases of cystic disease of the breast, reported by Greenough and Simmons, that the fact that a "recurrence of cystic disease of the breast or carcinoma occurred in breasts treated by partial operation in 12 out of 83 cases, or in 14 per cent.," justifies as a certain conclusion that only a partial operation is indicated. We believe that we should consider the point of view of the 14 per cent. who had recurrences. Are we justified in taking a 14 per cent. chance?

Benign Tumors.—As in the case of cysts, a discussion of the various types of what are generally classified as benign tumors is out of place here—in fact, to accept as a final dictum that any type of tumor is absolutely and finally benign is a dangerous conclusion. As Deaver[5] has stated: "Tumors of certain types having certain structure are constantly harmless; those of other types, having another structure, are persistently invasive, destructive, and constantly fatal. Unfortunately these are the extremes of a series between which lie many tumors that may or may not be harmful, or whose structures may fail to give a clue to their true disposition."

In our combined series of diseases of the breast, consisting

of 1264 cases, 161 (12.7 per cent.) were benign tumors, and 60 9 per cent of these were adenofibromata. The processes of development of tumors of this type may well lead us to question whether they are not potentially malignant. This question is

Fig. 299.—Large lipoma of left breast in married woman fifty-four years of age No previous history of possible precancerous condition except for abscess during first lactation Growth first noticed five or six years before consultation

emphasized by a study of the age incidence in our cases, as shown in Table 1

TABLE 1

Age Incidence of Pathologic Conditions of Breast

Age years	Benign, per cent	Malignant, per cent	Cysts, mastitis, etc., per cent
Under 20	3 2	0 2	0 4
20–25	16 5	0 7	7 1
25–30	15 7	1 9	11 2
30–40	28 3	15 5	29 4
40–50	24 4	31 1	41 8
50–60	8 7	27 6	8 2
60–70	3 2	17 7	1 5
Over 70	0 0	5 3	0 4

The comparatively high incidence in earlier years—*i. e.*, under thirty—of other than carcinomatous conditions, with the reverse comparison in later years, appears significant as a possible further indication of the potential malignancy of so-called benign conditions. In this connection a comparison of the age incidence of cysts and adenofibroma in particular made in a previous study is of interest (Table 2).

TABLE 2

Age, years	Cysts, per cent	Adenofibroma, per cent.
Under 20	0 0	4 8
20–25	0 0	19 0
25–30	14 8	28 6
30–40	33 3	9 5
40–50	38 9	28 6
50–60	11 1	9 5
60–70	1 9	0 0
70–80	0 0	0 0

Table 2 when compared with Table 1 would appear to indicate that whatever processes of involution at different age periods lead to the development of cancer, these processes are also potential in the production of cysts; whereas adenofibroma represents a more definitely precancerous condition.

A study of our total series has shown an apparent reversal during more recent years of the incidence relation between benign and malignant tumors It would seem that this might well be attributed to the fact that earlier consultation is sought by women who discover an abnormal condition in the breast, so that it is first seen and the operation performed while the tumor is still benign (Figs. 300, 301).

Hereditary Histories of Cancer.—Is there an inherited predisposition to cancer of the breast? In 17.8 per cent. of our cases an hereditary history of cancer is given. It is probable that for the present at least we must be contented with the accumulation of statistics upon which future conclusions can be based, and in the meantime take the point of view of Bashford (quoted by Hoffman)[6], that "The frequency of cancer as a cause of death is so great that few families of large size escape; and in

one of every two families either a parent or a grandparent will,

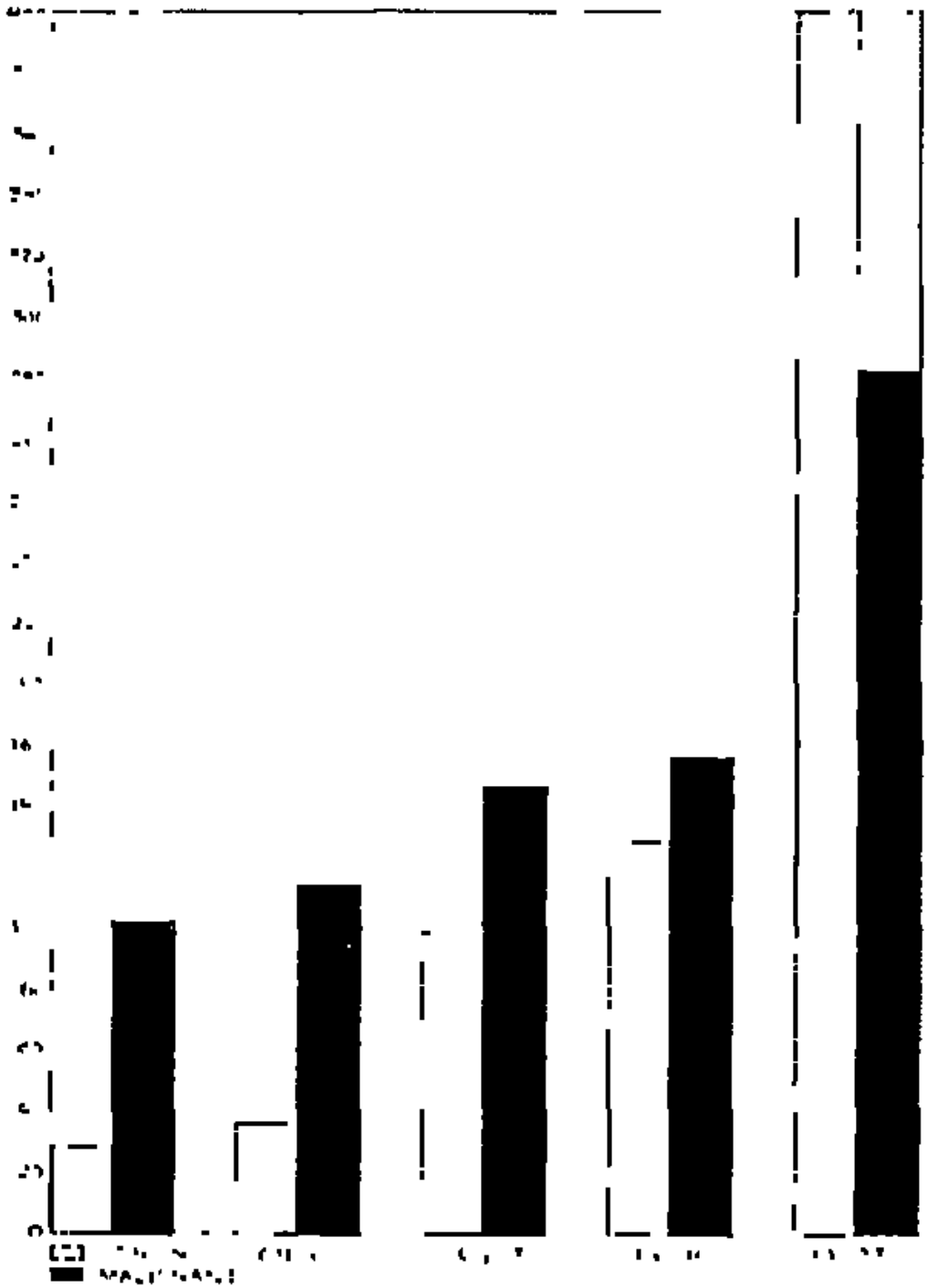

Fig 300.—Chart showing proportion of benign and malignant lesions of the breast examined during five-year periods. Statistics of Drs. Bunts, Crile and Lower, and their associates

on an average, have died of cancer, supposing such parents and grandparents to have died after thirty-five years of age," or in

other words, "The mortality from cancer is so great that, on an average, in one of two families either a parent or a grandparent

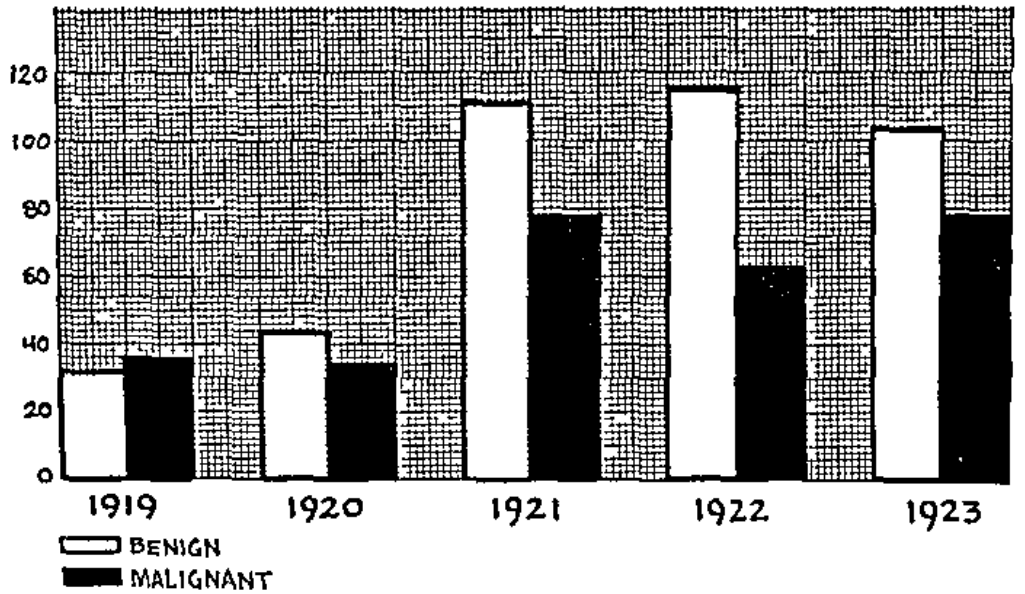

Fig. 301.—Chart showing the proportion of benign and malignant lesions of the breast. Statistics of Drs. Bunts, Crile and Lower, and their associates.

will have died of cancer without assuming hereditary predisposition."

The above discussions indicate the present uncertainty regarding the exact potentiality of each of the conditions cited.

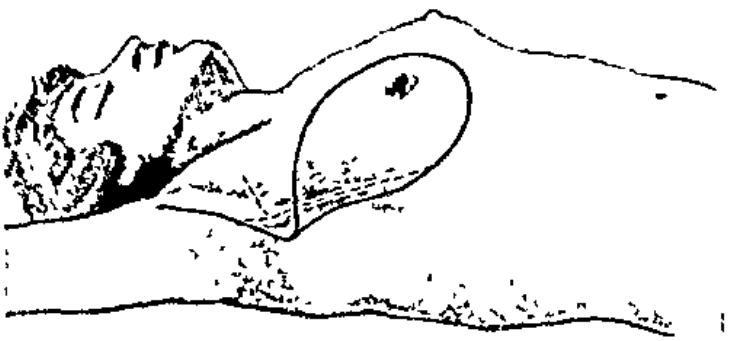

Fig. 302.—Line of incision for radical resection of the breast, with removal of the glands of the axilla.

In view of this uncertainty, what is to be our guide? Perhaps a line of procedure may be briefly summarized as follows: (1)

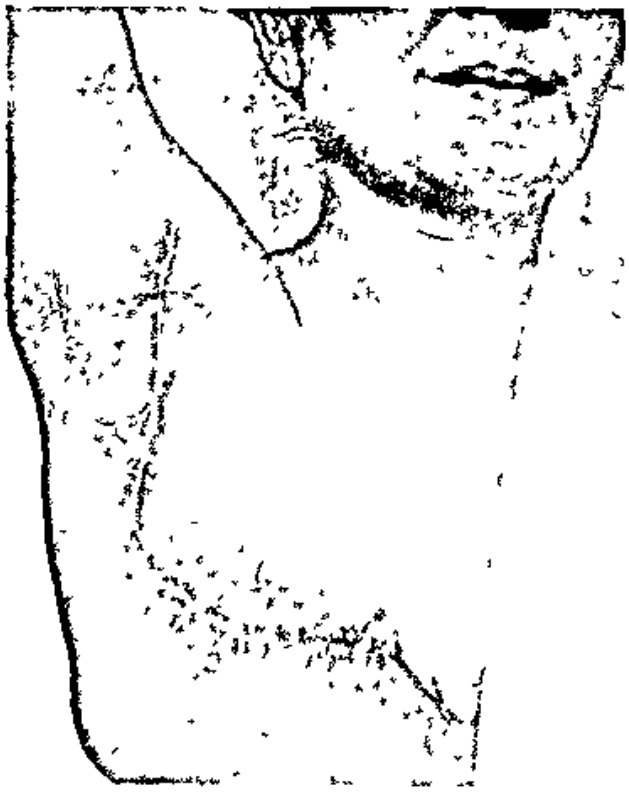

Fig. 303 —Appearance of scar and restoration of mobility of arm four months after operation

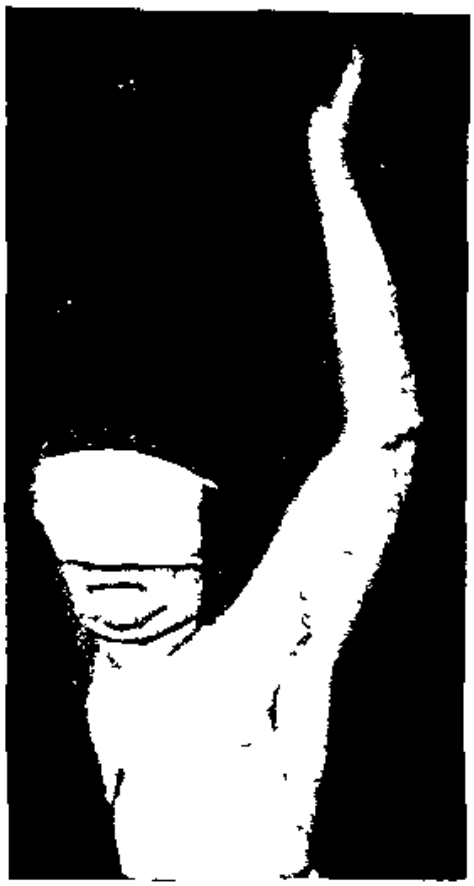

Fig. 304 —Practical disappearance of scar and mobility of arm three years after operation

Diagnosis and prognosis in each individual case must be based upon clinical experience; (2) avoidance of a mutilating operation unless reasonably assured that the prognosis demands it; (3) employment of a technic which will produce minimum scarring—a plastic method—this will minimize the reluctance of young women to undergo a resection of the breast (Figs. 302–304), (4) in doubtful cases a period of watchful waiting, with repeated frequent examinations; (5) exploration and removal of local lesions always.

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2 Knox, L C · The Relationship of Massage to Metastasis in Malignant Tumors, Ann. Surg., 75, 129–142
3 Deaver, J B., and McFarland, Joseph: The Breast: Anomalies, Diseases, Treatment, 1917, pp 274, 275.
4 Ibid , p. 290
5. Ibid., p 341.
6 Hoffmann, F. L Mortality from Cancer Throughout the World, Prudential Press, 1915, p 172.

W. E. LOWER

DEPARTMENT OF GENITO-URINARY SURGERY

THE RÔLE OF CERTAIN MECHANICAL DEVICES IN THE DIAGNOSIS OF DISEASES OF THE GENITO-URINARY TRACT

IN 1884 a French author, Poussin, in a monograph on vesical tumors, said that the only methods then available for genito-urinary examinations were three, viz.: (1) Hypogastric and rectal palpation; (2) catheterization of the bladder; (3) digital exploration of the bladder. Just before this date, however, in 1879 Nitze had made his memorable invention of the first practical cystoscope, the development of the fundamental principle in which progressed rapidly, with a corresponding extension of the possibility of accurate diagnosis. In 1893 Roentgen's monumental discovery put at the disposal of the urologist the greatest of all single diagnostic aids. As the result of the development of these two mechanical aids—the cystoscope and the *x*-ray—the possibility of establishing an accurate diagnosis of lesions of the genito-urinary tract has been extended beyond that in any other system of the body.

"Seeing is believing," and therefore the visualization of the stone, the inflammation, the tumor, the accumulation of pus, the presence of which has been suggested by the clinical history, the physical examination, the chemical analyses of the blood and the urine, the functional tests, brings the comfort of certainty to the urologist and of increased confidence to the patient.

In the apparent certainty of these mechanical aids, however, lies a certain danger, namely, that because of this very certainty regarding the presence of one or another local lesion we fail properly to evaluate the information regarding the patient as a whole, as well as regarding the functional capacity of the urinary

organs themselves which is provided by the history and the functional and chemical tests Therefore, while availing ourselves to the utmost of these more recently developed mechanical aids, of the x-ray in particular, it may be well occasionally to remember the achievements of earlier days, from the earliest records of medical history, through the Middle Ages, when physicians placed such dependence upon urinary examination that the urinal became the professional insignia, to the last century, just

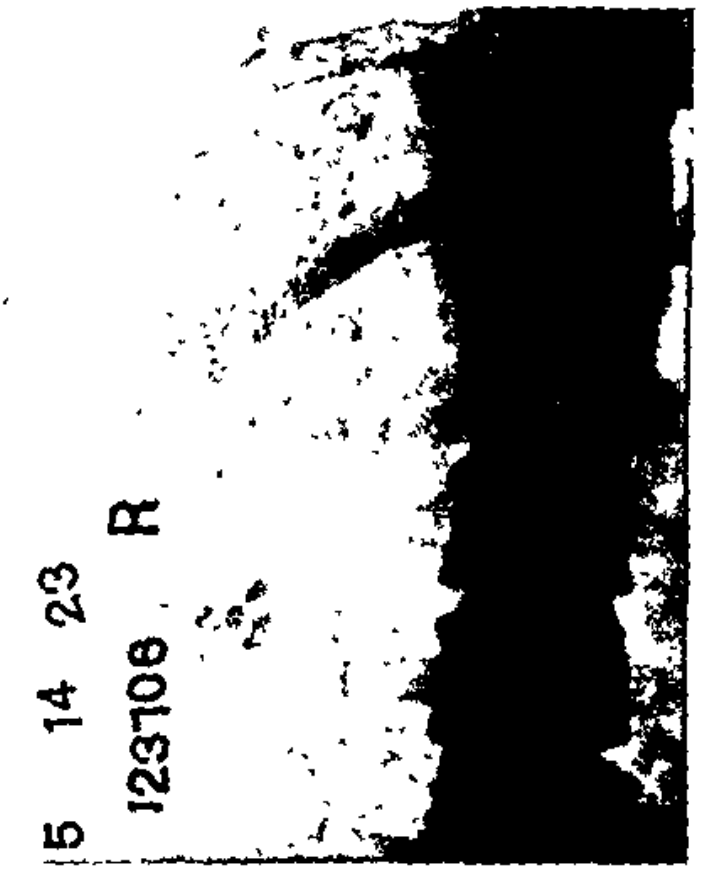

Fig 305.—Gall-bladder plate of Case I showing six shadows

before the invention of the cystoscope and the discovery of the x-rays

On the other hand, with the increasingly close liaison between the sciences of physics and of medicine, it may well be that additional instruments of diagnostic precision will be developed. Two such instruments which are now being developed in this Clinic will be described below

But just as to the mariner the compass, the sextant, the

barometer, the navigator's chart are indispensable aids, but are subservient to personal judgment based upon maritime experience, so to the urologist the various chemical and physical aids are indispensable, but must be subservient to clinical judgment.

The importance of close correlation between the laboratory worker, the roentgenologist, and the urologist is well illustrated by the following case histories·

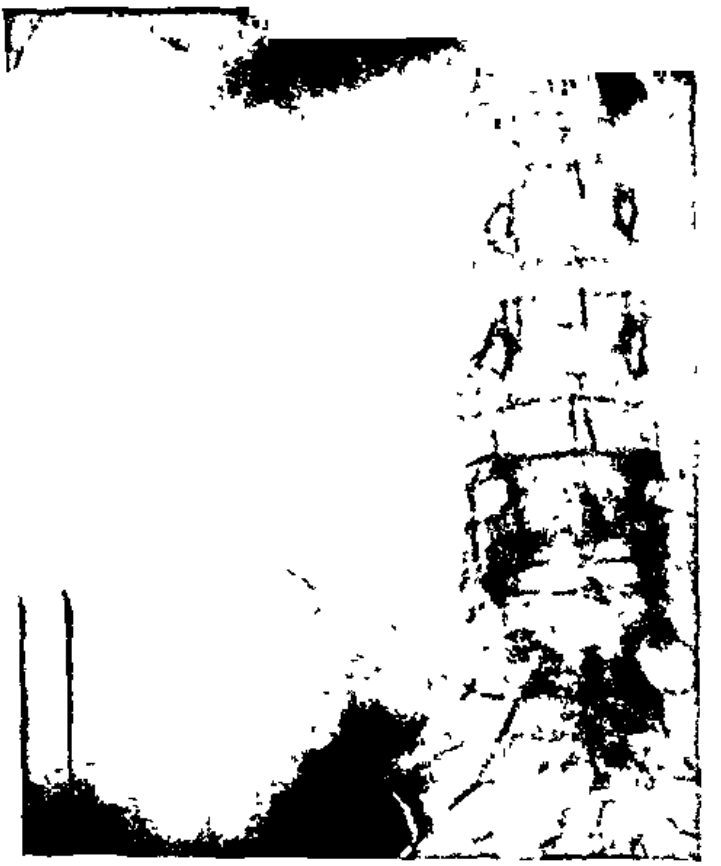

Fig. 306.—Kidney plate of Case I

Case I.—The patient, a woman thirty-nine years of age, came to the Clinic to seek relief from recurrent attacks of pain which she had experienced during the preceding five years. These attacks were always premenstrual. The pain was very severe over the right iliac crest, and discomfort extended down toward the right groin. The pain was usually relieved by the application of heat and by rest, but occasionally codein was required. Sometimes nausea accompanied the attacks of pain, but the patient never vomited and was always able to eat. She had neither diarrhea nor constipation. She had had no jaundice. During the duration of pain she experienced urgency and frequency of urination, but there was no pain, blood, or burning on micturition. There was no urinary disturbance between attacks.

organs themselves which is provided by the history and the functional and chemical tests Therefore, while availing ourselves to the utmost of these more recently developed mechanical aids, of the *x*-ray in particular, it may be well occasionally to remember the achievements of earlier days, from the earliest records of medical history, through the Middle Ages, when physicians placed such dependence upon urinary examination that the urinal became the professional insignia, to the last century, just

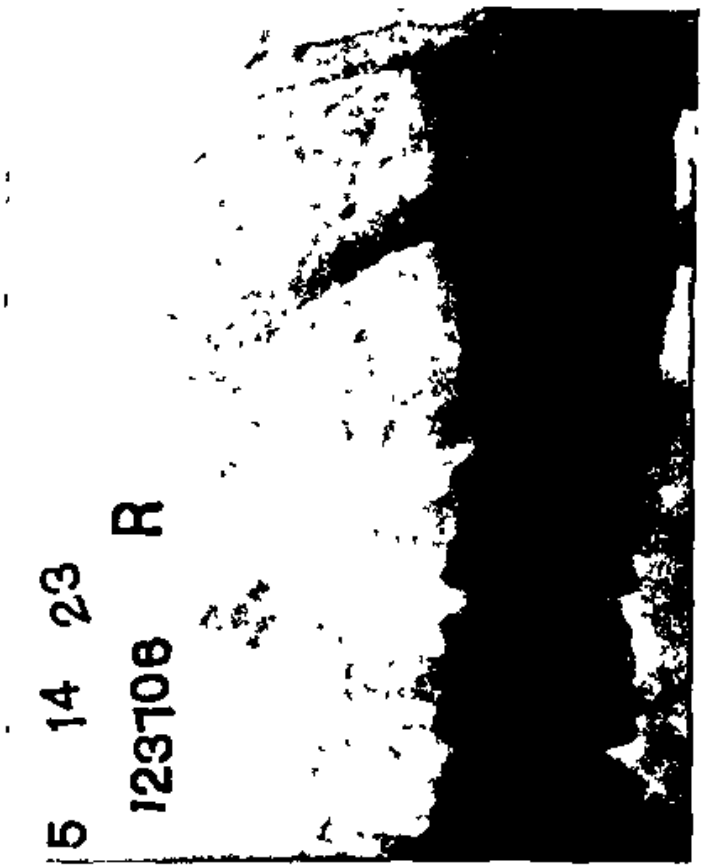

Fig 305 —Gall-bladder plate of Case I showing six shadows

before the invention of the cystoscope and the discovery of the *x*-rays

On the other hand, with the increasingly close liaison between the sciences of physics and of medicine, it may well be that additional instruments of diagnostic precision will be developed. Two such instruments which are now being developed in this Clinic will be described below

But just as to the mariner the compass, the sextant, the

At *operation* palpation of the upper pole of the right kidney indicated the presence of a cluster of stones in the upper calix, as indicated by the pyelogram A nephrotomy was done and six stones each about ¼ inch in diameter were removed (Fig 308)

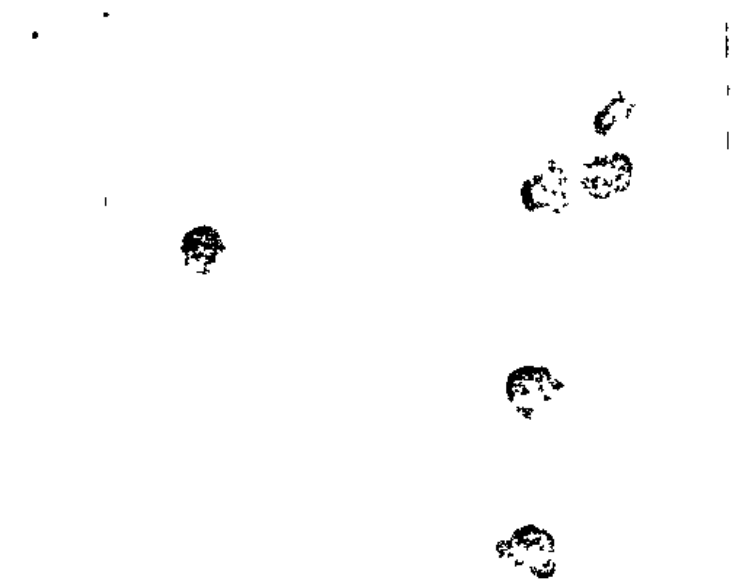

Fig. 308 —Six stones removed at operation on Case I.

Case II.—This patient, who was referred to me by Dr. P. G Krebs, was a woman fifty-nine years of age, who for five years had suffered from recurrent attacks of gastric pain, with nausea and vomiting, the pain being so severe as to require an anodyne for relief These attacks had recently been increasing in frequency and severity, and the patient thought the pain was radiating more toward the right side. In August, 1923 a severe attack of pain was accompanied by an increased temperature, and the condition was diagnosed as acute cholecystitis This attack lasted for nine or ten days. She had never had any hematuria. During these five years she had lost about 18 pounds in weight Just before her admission to the hospital she had had repeated attacks at short intervals, with pain radiating to the back and shoulder, and so severe as to require injections of morphin. There were no bladder symptoms.

It appeared evident that this was distinctly an uncomplicated case of cholecystitis with stones *x*-Ray plates, however, showed not only a number of shadows which undoubtedly were gall-stones, but a more dense shadow (Figs 309, 310), the location of which suggested that it might be a renal calculus To establish the diagnosis the ureters were catheterized and pyelograms taken, which showed only the upper calix of the kidney which gave the picture characteristic of a double ureter (Fig. 311) The dense shadow appeared on these plates also in the kidney region

At operation the kidney was exposed and double ureters were found, one of them extending to the upper pole of the kidney, as shown in the pyelograms A stone was found in the lower right kidney pelvis and was removed. The

Fig. 309.—Gall-bladder plate of Case II showing numerous small shadows anterior to right kidney and larger irregular shadow in region of kidney pelvis

Fig. 310.—Kidney plate showing same findings as those in Fig. 309.

peritoneum was then opened and the gall-bladder was found to be filled with stones, and a cholecystectomy was performed

The histories of these cases offer a clear-cut demonstration of the essential value of the *x*-ray in such cases. In the first, the negative laboratory tests and the lack of any significant findings in the cystoscopic examination might well have left us permanently in the dark regarding the exact cause of the recurrent at-

Fig. 311 —Pyelogram of right kidney in Case II, showing one major calix Characteristic picture of double ureter.

tacks of pain, significant though they were; and in the second case the classical symptoms of gall-stone colic might have prevented us from the further investigation which revealed the renal calculus.

The second case cited above illustrates the importance to the urologist of a general surgical training. With increasing specialization there is danger that the specialist may confine himself to the diagnosis and treatment of only such pathologic conditions as come specifically within his own field. For the

urologist, in particular, a general surgical training and experience is of special value In the above case, for example, had the urologist not had a general surgical experience and training, the removal of the gall-bladder would have required a second operation by another surgeon.

In all cases, but especially in such cases as that described above, in which a nervous patient is worn and discouraged by

Fig 312 —Cystoscopic table equipped for taking roentgenograms

repeated attacks of pain and the various essential steps in the examination, we have found it of great aid to have the equipment for taking the roentgenogram incorporated in the cystoscopic table, thus avoiding for the patient the annoyance and discomfort of a second preparation and catheterization (Fig. 312).

In collaboration with the department of biophysics we

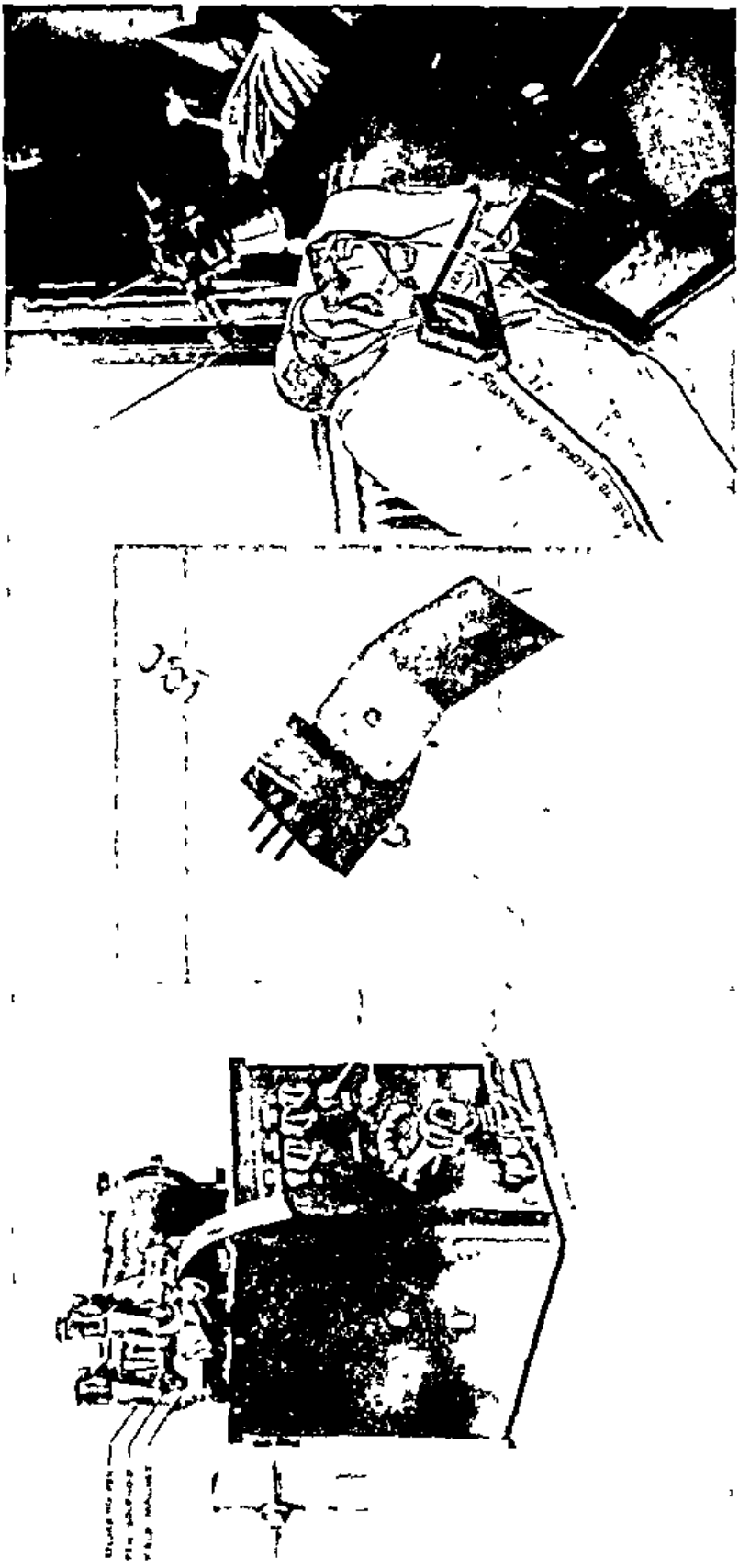

Fig. 313.—Urine recording apparatus.

have devised two pieces of apparatus, the clinical application of which is now being worked out. One of these is based upon the assumption that since variations in function will in accordance with physical laws presumably be accompanied by variations in temperature, it might be possible to identify the infected kidney in obscure cases by a comparison of the temperature of the two kidneys Thermocouples capable of measuring variations in temperature to within .005° C have, therefore, been constructed in our electromechanical department The connecting wires of these are passed through ureteral catheters,

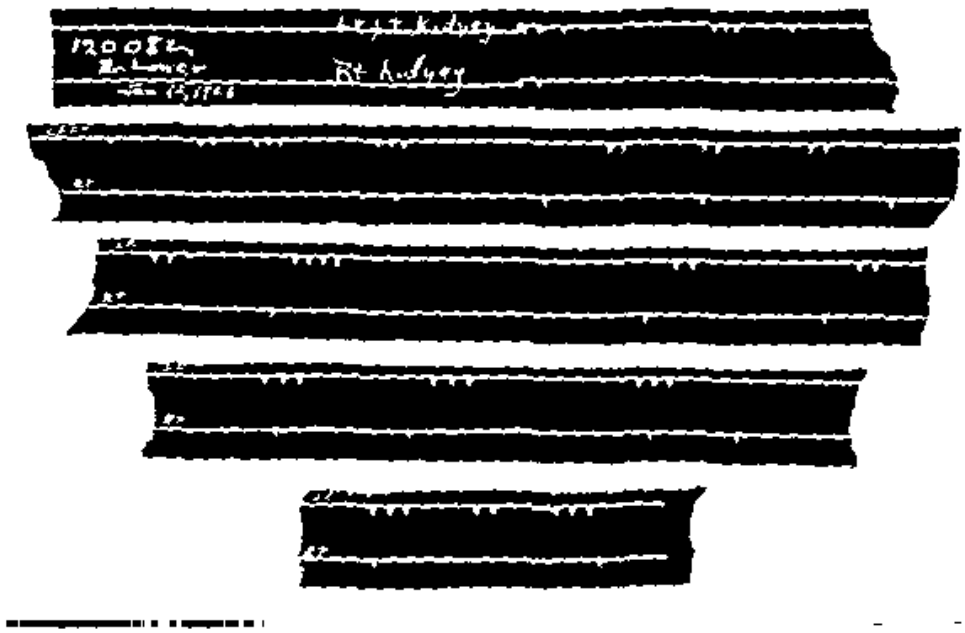

Fig 314 — Urine excretion record made with apparatus shown in Fig 313

thus admitting of their passage to the kidney. These have been tried in 2 cases—one a case of infected intermittent hydronephrosis due to calculus, the other an infection also due to a calculus. In the first of these the temperature was 041° C. higher on the infected side (right) than on the other; in the second case the temperature was 050° C higher on the infected side (left)

We have also profited by the aid of our departments of biophysics and of electromechanics in the construction of a device whereby simultaneous records of the excretion of urine from the two kidneys can be made automatically (Fig 313).

The record secured in one case is shown in Fig. 314 The difference in the urinary flow from the two kidneys is at once apparent, and while the true significance of these variations remains to be determined, it is of interest to note that in this case there was some pain in the back over the left kidney, and that the specimen from the left kidney showed a faint trace of albumin, in contrast to the entirely normal findings in the specimen from the right kidney.

In conclusion I would emphasize again that these newer aids must be used only in conjunction with the other examinations—complete physical examination and laboratory tests of the urine and blood. The results of the cystoscopic examination and of the urinalysis, the measurements by means of the thermocouple and the record of urine excretion—should the last two finally prove efficient and dependable methods—are to be interpreted together with the history by the clinical judgment of the urologist.

W. E. LOWER AND G. W. BELCHER

DEPARTMENT OF GENITO-URINARY SURGERY

NOTES ON PYELOGRAPHY

A STUDY of the pyelograms made at the Cleveland Clinic during the past year has revealed several points of such interest and value to us that it has seemed worth while to record them here.

We have found that most of our mistakes occurred in cases in which a short-cut technic was used to arrive at a presumably easy diagnosis. Thomson Walker recently outlined a very good routine for the practice of pyelography, but there are a few points which we would like to stress since their importance has been emphasized by our experience. These are: (1) the condition of the intestinal canal at the time of examination, (2) the preliminary stereoscopic study of the entire urinary tract, and (3) the amount of fluid to be injected when making the pyelogram.

In the roentgenographic examination of the urinary tract the investigator, especially if he is pressed for time, is apt to miss a calculus, even though the Potter-Buckey diaphragm is used. In all cases, therefore, the unexplained presence of red blood-cells in the urine should make one suspicious of calculus. A radiogram partially blurred with gas makes it very difficult to identify the deceptive shadows of small ureteral calculi, and the finer defects shown on the pyelogram will often be missed when the examination is made under such conditions. It is very important, therefore, that the intestines be empty in order that fecal concretions may not be mistaken for stones. We have found that in these cases the administration of a high colonic enema the evening before and another on the morning of the examination is more satisfactory than catharsis.

A thorough preliminary stereoscopic study of the urinary tract, the associated organs, and the neighboring parts of the skeleton is as important as the condition of the intestines. By this means we may discover the presence of congenital malformations and chronic inflammatory or malignant disease of the spine, ribs, pelvis, and their respective articulations Except in very obese subjects the stereoscopic plates will always show the outline, size, and position of the kidneys In cases in which the urinalysis and functional findings are uncertain or confusing, the

Fig 315 —Duplication of urinary tract suggested by unusual kidney outline Upper pelvis filled with 15 per cent sodium iodid

presence of tuberculous renal calcifications and enlarged kidneys, the latter associated with shadows in the courses of their ureters, is of great value in determining which kidney should be subjected to a pyelographic examination. Furthermore, when the preliminary plates show a suspicious shadow in front of a bone, the subsequent radiographic and cystoscopic procedures can often be made of diagnostic value only by taking plates at another angle, so as to shift the position of the shadow to a field not obscured by bone.

A

B

Fig 316.—Pyelograms showing the importance of underdistention of the kidney pelvis: A, False impression of filling defect given by overlapping of minor calices in completely filled pelvis B, Same pelvis clearly outlined by underdistention

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superimposition of minor calices is usually, though not invariably, very clear. Complex pelves—*i. e.*, those with a large number of minor calices—are particularly troublesome. We have noticed that this type of pelvis is especially apt to be present in cases of essential hematuria. Figure 317 is a pyelogram of a case in which an apparently essential hematuria recurred for the first time twelve years after a complete splitting of the kidney.

The Pyelogram in Cases of Renal Malignancy.—The identification of a renal neoplasm before the presence of a palpable

Fig. 318.—Spider pelvis. (From Braasch's Pyelography, Fig 249, p 261.)

mass is demonstrable is one of the valuable accomplishments of pyelography. Three types of malformations of the renal pelvis are produced by tumors—the spider pelvis, the retracted or cut-off calix pelvis, and the pelvis which shows only a filling defect. These malformations may be due to other causes, however, so that the presence of any one of them cannot be considered as final evidence of a renal tumor.

The "spider pelvis" (Fig. 318) is nearly always malignant. On the other hand, pelves of the retracted or cut-off calix type are very deceptive. During the past year we have removed two

kidneys in which this deformity had been demonstrated, subsequent pathologic examination showing them to be non-malignant. In each of these cases the patient had suffered from attacks of hematuria and was losing weight The pelves of this type, which are shown in Figs. 319–321, present a similar appearance, and yet the pathologic conditions differ. In the kidney shown in Fig. 319, taken from Braasch's "Pyelography," the retracted pelvis is due to a renal tumor. Figure 320, from our series, was obtained in a case of stricture of the infundibulum

Fig 319—Retracted calix, renal tumor (From Braasch's Pyelography, Fig. 244, p 257)

of the superior calix, a heminephrectomy, which entirely relieved the patient of her symptoms, showed this to be a case of hydronephrosis of the superior calix The kidney shown in Fig 321 was found after removal to be normal, though its function was slightly decreased, and distention after removal gave a normal pelvic outline This patient had been losing weight and had had intermittent attacks of hematuria. A close examination of this pyelogram shows that the tip of the ureteral catheter is pressed rather sharply into the wall of the superior

Fig. 320.—Hydronephrosis caused by stricture of infundibulum: A, First pyelogram. B, Second pyelogram C, Superimposition of pyelograms A and B

Fig. 321 —Filling defect caused by tip of ureteral catheter pressing into the wall of the superior infundibulum Normal kidney found at operation

Fig 322 —Filling defect caused by renal calculus

infundibulum, thus preventing the fluid from entering the pelvis. Our experience in this case shows that in cases in which the retraction defect and loss in function are very slight, es-

Fig 323.—Injection of kidney after removal, showing large tuberculous abscess

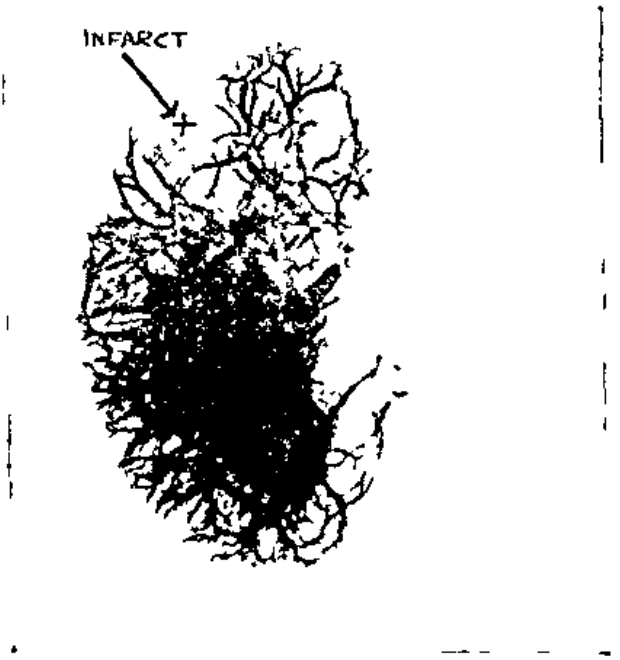

Fig. 324.—Injection of kidney after removal, showing infarct of old tuberculous lesion.

pecially when the results of other examinations are negative, further investigation is required. In such a case exploration is indicated when the phenolsulphonephthalein output progressively decreases, with a progressive increase in the deformity.

A pelvis which shows a filling defect, although not pathognomonic of tumor, as is the spider pelvis, nevertheless is never normal. Such a case, however, should always be checked to rule out technical defects These filling defects may be due to papillomata, to calculi, or to cysts Figure 322 shows a pyelogram of the only case of this type in our series In this case at operation the deformity was shown to be due to a calculus.

The *x*-ray study of the injected kidneys after their removal is very interesting. Thus in Fig. 323 is shown a large cortical abscess, and in Fig 324 the infarct of an old tuberculous lesion, neither of these lesions being demonstrable in the pyelograms

Fig. 325 —Injection of kidney after removal, showing area of infarction produced by cortical calculi

Figure 325 shows the area of infarction produced by cortical calculi which although not as serious as calculi which are free in the pelvis are nevertheless definitely destructive However, these findings while interesting have no practical value, as the injection of the blood-vessels with opaque solutions *in vivo* is impossible

The matter of prime importance is the necessity of utilizing every diagnostic measure at our command in the study of lesions of the genito-urinary tract, of studying the findings in each examination in the light of the others; and, above all, of relating the laparotomy and *x*-ray findings to the clinical history.

JOHN PHILLIPS

DEPARTMENT OF INTERNAL MEDICINE

SUBPHRENIC ABSCESS

THE term *subphrenic abscess* is applied to any collection of pus which is in contact with the under surface of the diaphragm, with the exception of pus in the liver or spleen. Many of the important symptoms and physical signs of this condition which frequently follows acute inflammation of the various organs within the abdominal cavity are illustrated by the following case history:

The patient, a man thirty-five years of age, was seen on March 9, 1924, in consultation with Dr. E. J. Marsh, of Canton. The primary symptoms of his illness, which began four weeks previous to my visit, were indefinite pains in the lower right quadrant of the abdomen, with some tenderness and slight rigidity in the region of McBurney's point. At that time his temperature ranged from 101° to 102° F , but, as on the following day the tenderness and rigidity had almost disappeared, operation was not advised Two days later there was some tenderness below the right costal margin in the region of the gall-bladder, but this did not persist One week following the onset of his illness he began to have chills, particularly in the afternoon, and at the same time a septic type of temperature developed, with a wide range of from 98° to 106° F. This irregular fever, with the chills and sweats, together with progressive weakness, continued until the time of my visit When I saw him he complained of considerable soreness over the liver, but had no acute pain. At times he was slightly delirious. Various urine examinations had been made, but, beyond a faint trace of albumin and the presence of indican, nothing abnormal was found. He had a leukocytosis of 20,000.

The physical examination was made shortly after a chill. The patient was perspiring freely and looked pale and extremely ill. He was breathing quietly, with a respiratory rate of 32. There were no important physical findings except those in the chest and abdomen Inspection of the chest disclosed some bulging of all the interspaces on the right side below the fifth rib, so that the circumference of the lower portion of the right side was greater than on the left. Litten's diaphragm phenomenon was absent on the right, but present on the left side. The lower portion of the right side of the chest did not expand as well as the left side Palpation confirmed these observa-

tions, and on pressure over the lower portion of the right axilla some tenderness was elicited The right costal margin moved outward, but the excursion was not as extensive as on the opposite side Tactile fremitus was diminished on the right side below the fourth rib in front, in the axilla, and below the angle of the scapula Percussion revealed a dome-shaped area of dulness extending as high as the third interspace in the right sternal line, to the highest point in the axilla, and posteriorly to the angle of the right scapula The heart was not displaced to the left On auscultation on the right side below the upper limits of the area of dulness the breath sounds, the whispered and the spoken voice sounds were feebly heard No coin sound could be elicited The heart sounds were clear, the pulse-rate 110, the blood-pressure, systolic 120, diastolic, 70

Palpation of the liver, which caused some discomfort to the patient, showed that its lower border extended about 3 cm below the right costal margin No tenderness and no masses could be felt elsewhere in the abdomen. The spleen was not palpable

The diagnosis of subphrenic abscess was made, and it was thought that in all probability the condition was secondary to an inflammation of the appendix On the following day the patient was operated upon by Dr. Marsh, who found an encapsulated abscess containing about 10 ounces of pus below the right dome of the diaphragm. The condition of the patient was improved for a few days after operation, but he later developed an empyema and died.

In a general discussion of subphrenic abscess two forms must be considered· (1) Simple subphrenic abscess without any contained air, (2) subphrenic pyopneumothorax containing air. These two varieties are found in about equal numbers

Etiology.—There are many causes of simple subphrenic abscess, the most frequent being appendicitis. Subphrenic abscess may follow an inflammation of an appendix situated retrocecally, the infection in such a case having only a short distance to travel, as the tip of the inflamed appendix may extend almost to the right lobe of the liver. In other cases the infection from the appendix may travel intraperitoneally along the paracolic groove to the right kidney pouch, and extend upward over the liver A subphrenic abscess may follow a pylephlebitis, complicating appendicitis; or it may occur as a residual abscess, the result of a wide-spread peritonitis. Occasionally an abscess of this character is situated beneath the left dome of the diaphragm, but in the majority of cases a subphrenic abscess which follows appendicitis is situated beneath the right dome of the diaphragm.

A suppuration in the liver, such as a tropical abscess, a suppurating hydatid cyst, or a localized abscess from cholangeitis or pylephlebitis may cause subphrenic abscess.

The perforation of a duodenal or gastric ulcer may be the primary cause of a subphrenic abscess As a rule the perforation of a duodenal ulcer causes general peritonitis, but in some cases the pus makes its way to the right kidney pouch, and later extends above the liver. The perforation of a gastric ulcer into the lesser peritoneal cavity usually causes a subphrenic pyopneumothorax, but occasionally, if the perforation is small, a non-gaseous abscess may result.

Among other causes of subphrenic abscess may be mentioned pericolic abscess, suppurations about the pancreas, abscess of the spleen secondary to infective emboli or trauma, retroperitoneal suppuration originating in the kidneys or in diseased vertebræ or ribs, and occasionally suppuration in the fallopian tubes may extend up the paracolic groove

In rare instances an empyema may make its way through the diaphragm and cause a subphrenic abscess. I saw such a condition a few days ago in a man forty years of age who had been ill for two months with pneumonia complicated by pericarditis The pneumonia involved the base of the left lung, and the dulness in this area persisted, but owing to his extremely weakened condition his physician, though he suspected empyema, was afraid to operate. The patient developed a subphrenic abscess on the left side, with definite bulging below the left costal margin, from which a large amount of pus was obtained by incision and drainage (Fig 326). It is curious that this complication does not more frequently occur when one considers how often a subphrenic abscess makes its way through the diaphragm into the pleural cavity.

As indicated above, the majority of subphrenic abscesses are situated between the liver and the right cupola of the diaphragm, but in a small proportion of cases the abscess lies beneath the left cupola of the diaphragm and above the spleen and stomach, in which case the abscess is limited on the right side by the lateral and falciform ligaments of the liver and by

adhesions. Abscesses limited to the lesser peritoneal cavity and due to perforation of the stomach are situated in the epigastrium In cases of subphrenic abscess on the right side the right lobe of the liver is depressed and rotated downward so that the bile-ducts may be compressed or kinked, causing jaundice

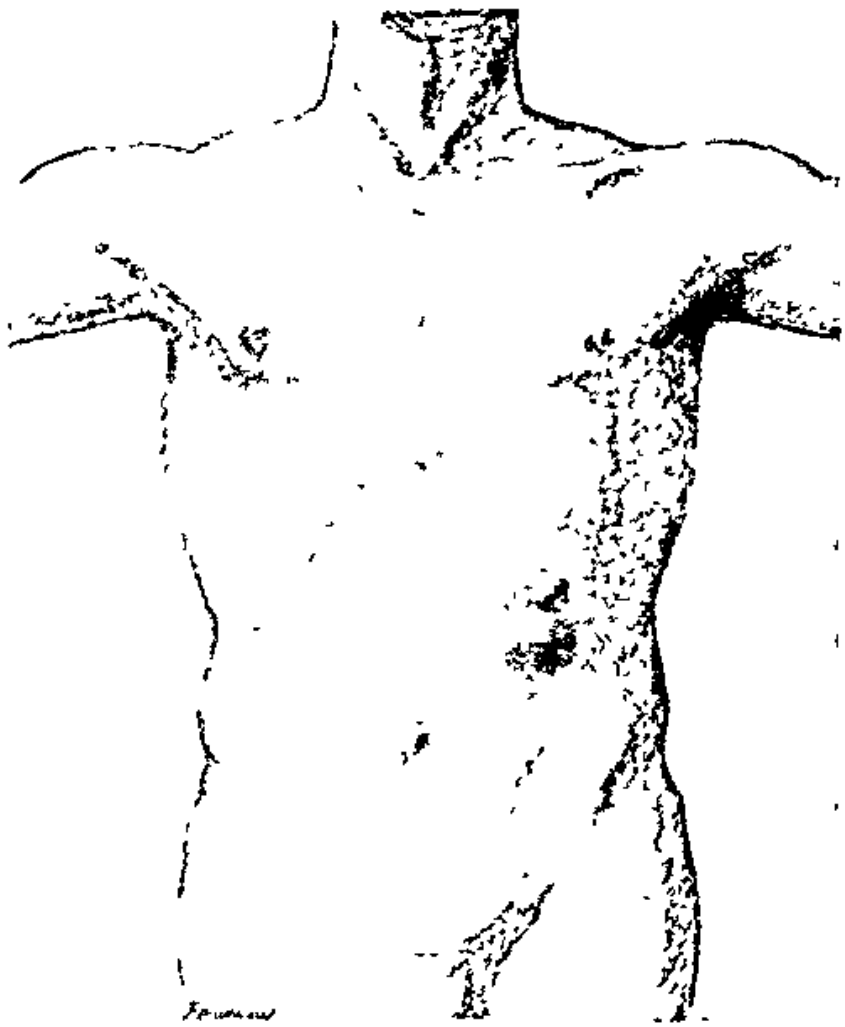

Fig 326.—Diagrammatic drawing, showing pointing of subphrenic abscess below left costal margin

If left untreated, a subphrenic abscess will usually perforate the diaphragm, causing an empyema; or it may even involve the lung and rupture into the bronchus I saw one case in a man fifty years of age in which an abscess which pointed in the epigastrium and was drained, also involved the lung and ruptured into the bronchus The epigastric incision closed, but following

this for ten years, at intervals of two or three weeks, he had attacks of chills and fever which lasted for three or four days and were relieved by the coughing up of a large quantity of foul-smelling pus.

A subphrenic abscess may perforate into the stomach or colon, but this occurrence is rare. Rupture into the peritoneal cavity is a very grave event, and is usually fatal External rupture also has been described.

The symptoms of subphrenic abscess vary according to the location of the abscess and according to the primary disease. Thus an abscess situated below the right cupola of the diaphragm may resemble an intrahepatic abscess, while one located in the lesser peritoneal cavity may present features resembling those of a pancreatic cyst. The onset in many cases is gradual. This is particularly true in cases following an operation for an appendiceal abscess in which the fever, rapid pulse, chills, and sweats continue until abnormal signs at the base of the right lung develop. In other cases, as in those due to perforation of the stomach, the onset, with pain, chills, and fever, may be very sudden.

In the majority of cases the physical signs of subphrenic abscess may simulate thoracic disease, while in other cases the signs are mainly abdominal. The temperature is elevated, with wide variations between the morning and afternoon temperature. The pulse is rapid and the leukocyte count varies from 15,000 to 30,000. The lower portion of the chest on the affected side may show bulging, and in cases in which there is a large accumulation of pus there may be edema of the chest wall. The expansion of the chest is restricted, though the outward movement of the costal margin is not interfered with as much as in cases of pleurisy with effusion. There is a dome-shaped area of dulness above the liver, usually higher posteriorly. The tactile fremitus is decreased over this area, while the breath sounds, though distant, may be bronchial in character because of the compression of the lung. At times a pleural friction-rub can be heard. The heart shows little or no displacement.

In cases in which the abdominal signs predominate the

lower edge of the liver is depressed and there are tenderness and rigidity below the liver and in the right costovertebral angle. Tenderness and rigidity may be present also on the left side, with definite bulging, as in the patient mentioned above in whom the abscess pointed below the left costal border. If these cases are untreated death usually results from exhaustion, or else the abscess may burst into one of the abdominal viscera, the pleura, the lung, or even into the pericardium; or occasionally it may rupture externally through the ribs or the abdominal wall.

The roentgenogram may be of great aid in establishing the diagnosis, the high position of the diaphragm on one side, with its limitation of movement being indicated by a subphrenic dark area

In the differential diagnosis the greatest difficulty is experienced in distinguishing subphrenic abscess from empyema. The history of the patient, the rigidity and tenderness of the upper abdominal muscles, with depression of the liver, the absence of displacement of the heart, and the lessened interference with the outward movement of the costal margin are all signs which indicate a subphrenic abscess

An accumulation of pus in the lesser peritoneal cavity produces a rounded swelling in the epigastrium which may simulate a pancreatic cyst The history of symptoms which indicate gastric disease, with the sudden onset of pain with chills and fever, would suggest an abscess rather than a cyst

Subphrenic pyopneumothorax may show symptoms and signs which suggest pneumothorax Thus there may be dull and tympanitic areas in the chest, amphoric breathing, metallic tinkling, and the coin sound, as in pneumothorax

The differentiation of subphrenic pyopneumothorax from pyopneumothorax may be very difficult In the former the history will usually indicate the presence of some abdominal lesion, such as perforation of a gastric or duodenal ulcer or of the appendix The liver is depressed and the lower portion of the lung is compressed There may be resonance or tympany above the level of the compressed lung, and movable dulness

below, with amphoric or diminished respiratory murmur, metallic tinkle, coin sound, and succussion splash. In pneumothorax there is less interference with mobility of the chest and the costal margin on the affected side may move outward. In subphrenic pyopneumothorax the heart is only slightly displaced. A roentgenogram will show that the diaphragm is pushed upward, with a relatively clear space in the costophrenic sinus The pus obtained by puncture often has a fecal odor. The exploratory needle if it passes through the diaphragm will be tilted upward and downward during respiration. Jaundice is often present.

The **treatment** of subphrenic abscess is surgical and consists in opening and draining the abscess cavity.

JOHN PHILLIPS

DEPARTMENT OF INTERNAL MEDICINE

THROMBOSIS OF THE CAVERNOUS SINUSES

THROMBOSIS of the cavernous sinuses as a rule follows infections of the face, the nasopharynx, the cranial sinuses, the teeth, and, in many instances, of the middle ear. In the following case septic thrombosis of the cavernous sinuses followed an acute otitis media:

The patient, a little girl aged six, was seen in consultation May 26, 1924. The history stated that about twelve days previous to my visit she had been taken ill with high fever due to an acute inflammation of the nasopharynx. Three days afterward she developed an acute otitis media so that the ear drum on the right side had to be punctured Since then the drainage from the ear had been free, there had been no tenderness or swelling over the mastoid, but the temperature continued to show an elevation varying from 100° to 103° F Until twenty-four hours before my visit the child did not appear very ill, in fact, her temperature seemed to be gradually getting lower Nothing unusual had been noted about her eyes.

About twenty hours before my visit the condition became worse, the temperature gradually mounting to 104° F., and a few hours later to 106° F. The patient became quite delirious and later passed into a state of coma.

Physical Examination—The child was very pale and looked extremely ill. Her breathing was Cheyne-Stokes in character. The right ear was discharging freely, there was no swelling or tenderness over the mastoid, and there was no sagging of the posterior wall of the auditory canal. There was no tenderness or swelling along the line of the jugular vein on the right side There was very marked proptosis of the right eyeball, which was fixed, and the pupil was moderately dilated and fixed The veins of the upper eyelid were much distended and there was definite chemosis of the conjunctiva. General orbital edema was present and there was considerable swelling over the bridge of the nose. There was some proptosis of the left eye, with orbital edema, which was not as extensive as on the right side (Fig. 327). The tongue was coated and there was considerable redness of the nasopharynx There was no evidence of any disease of the lungs, heart, or abdomen. The tendon reflexes were normal. The urine showed a trace of albumin and a few casts. The leukocytes numbered 20,000.

The patient died a few hours after I saw her The infection in this case, in all probability, reached the cavernous sinus through the superior petrosal sinus This may occur with or without mastoid involvement.

Thrombosis of the cavernous sinus is a comparatively rare condition Dorland Smith in 1918, after a careful study of the literature, found 140 reported cases Of these, 56 (40 per cent.) were secondary to ear infections, 49 (35 per cent) were secondary

Fig 327 —Sketch showing appearance of proptosed eyeball in a case of thrombosis of the cavernous sinus

to face or orbital infections, 18 (13 per cent) were secondary to mouth and throat infections; and 13 (9 per cent) were secondary to nasal infections The percentage of recovery among these reported cases was 7 per cent My personal experience covers 4 cases, 1 secondary to extraction of an infected tooth, 2 secondary to maxillary sinus infection, and the 1 above mentioned, secondary to infection of the middle ear. Of these 4, 1 recovered

The symptoms and physical signs of cavernous sinus thrombosis are so dependent upon the anatomy of the sinuses that a short discussion of the latter is important.

The cavernous sinuses are paired sinuses extending along the sides of the body of the sphenoid bone from the sphenoidal fissure in front to the apices of the petrous portion of the temporal (Fig. 328). Each measures about 2 cm. in length and has a diameter of about 1 cm. and is almost quadrilateral in cross-section. It is traversed by numerous trabeculæ, by the internal carotid artery, and by the abducent (sixth) nerve The oculomotor, trochlear, ophthalmic, and maxillary divisions of the tri-

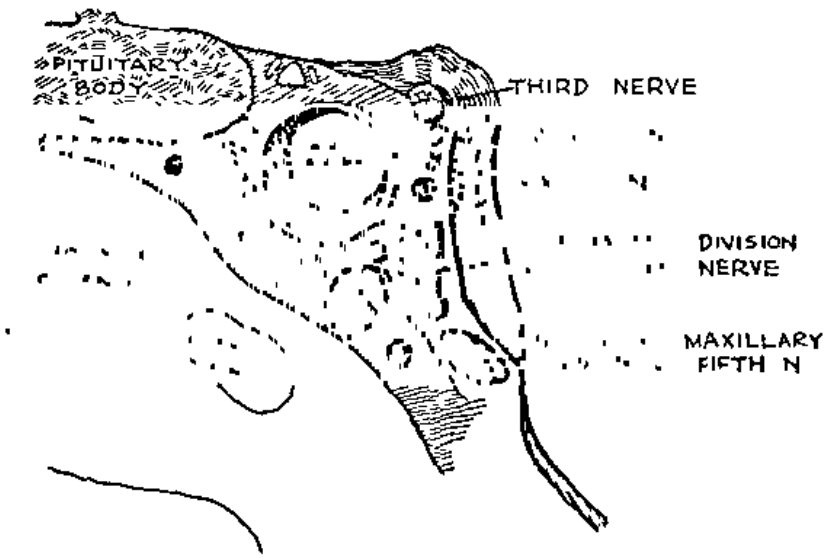

Fig 328.—Frontal section through the right cavernous sinus. (Redrawn from Gray's Anatomy, 1913, p. 725.)

geminus are embedded in its outer wall from above downward in the order named. The cavernous sinuses receive the ophthalmic veins at the sphenoidal fissures. They also communicate with the veins from the pterygoid and pharyngeal plexuses, with veins from the under surface of the frontal lobe of the brain and with the middle cerebral veins. Posteriorly they communicate with the superior and inferior petrosal sinuses. There are usually two, sometimes three, intercommunicating channels between the cavernous sinuses on the two sides. These channels form the circular sinus, and this communication readily explains the frequent occurrence of bilateral symptoms (Fig. 329).

It can be readily seen from the above description that cavernous sinus thrombosis may be secondary to infections of the face, such as a carbuncle, to inflammations of the nose, nasopharynx or paranasal sinuses, to inflammations of the ear and mastoid, to abscessed teeth or alveolodental periostitis, and to osteomyelitis of the frontal diploic tissue

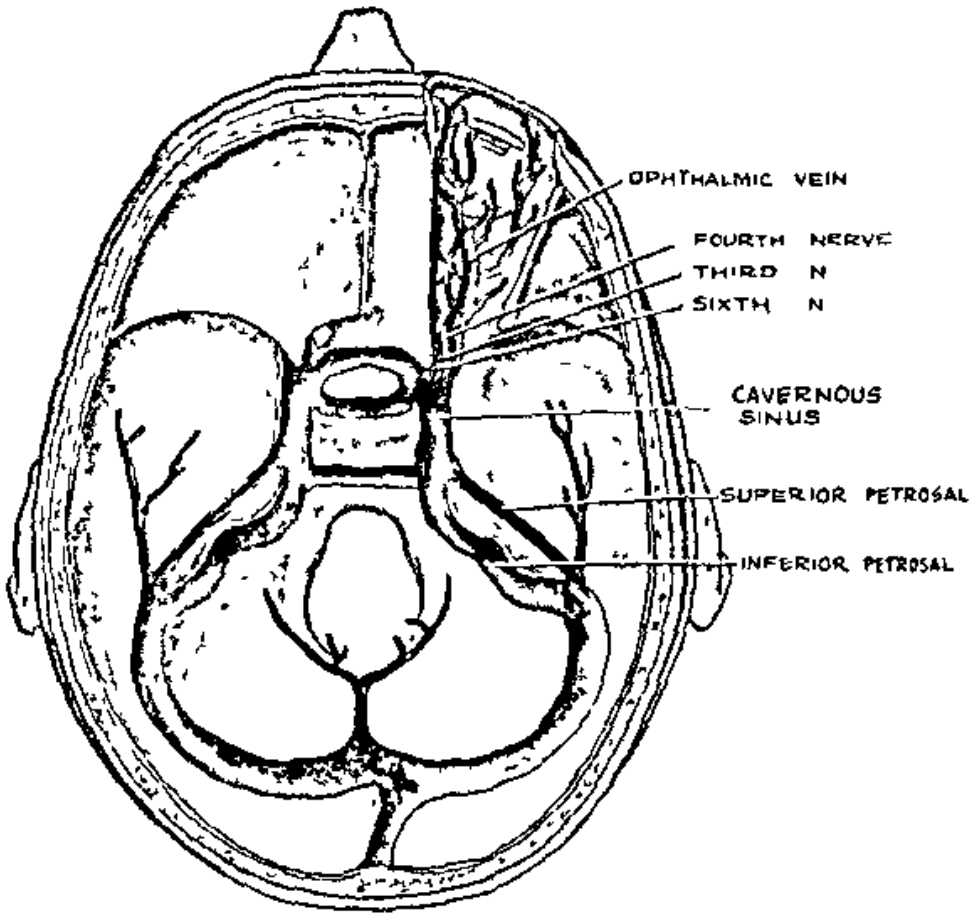

Fig 329.—The sinuses at the base of the skull (Redrawn from Gray's Anatomy, 1913, p 726)

The symptoms and physical signs of cavernous sinus thrombosis fall into two groups. (1) General symptoms such as general sepsis, headache, chills, fever, delirium, loss of appetite, constipation, general aching, rapid pulse, leukocytosis, (2) pressure symptoms involving the ophthalmic and the retinal veins, and the third, fourth, fifth, and sixth cranial nerves

Obstruction of the ophthalmic veins causes progressive swelling of the orbit, with dilatation of the veins of the eyelid,

followed by steadily increasing proptosis, with chemosis of the conjunctiva. Pressure on the nerves interferes with the movements of the eyeball. The sixth nerve, because of its course through the sinus, is the first nerve involved, with resultant paralysis of the external rectus muscle of the eye Later, involvement of the third and fourth nerves causes ptosis, interference with the upward movements of the eyeball, and finally complete fixation of the eyeball, with dilated pupil. Anesthesia of the cornea is sometimes present, this being due to involvement of the fifth nerve. One of my patients complained of intense pain in the face in the region of distribution of the fifth nerve. Ophthalmoscopic examination shows dilatation of the retinal veins, occasionally hemorrhages into the retina, and at times slight swelling of the optic disk.

The course of the disease is usually quite short, the majority of cases living only two or three days from the onset.

Many conditions might cause difficulty in differential diagnosis. Among these may be mentioned arteriovenous aneurysm, orbital growths, orbital periostitis, and cellulitis. The last named condition is the one that is the most difficult to differentiate, but in cellulitis the systemic disturbance is slight or absent; the movements of the eyeball are only slightly interfered with, and the proptosis is limited to one eye, while in sinus thrombosis both eyes soon show proptosis.

Surgical treatment has been attempted in cases of thrombosis of the cavernous sinuses, but so far has been unsuccessful.

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Department of Roentgenology

THE APPLICATION OF THE *x*-RAYS IN THE DIAGNOSIS OF GALL-BLADDER DISEASES

The radiologist is frequently asked, Is an *x*-ray study of the gall-bladder worth while? To this query we give an affirmative answer, provided the proposed study is sufficiently inclusive We mean by this that a complete study of the gall-bladder should include a series of properly made films of the gall-bladder, one at least of the right kidney and ureter, films of the stomach and duodenum after a barium meal, and a study of the hepatic flexures of the colon. Any one of these may give us sufficient evidence to warrant a diagnosis of a pathologic gall-bladder Through the work of Cole and Gerge the *x*-ray study of the gall-bladder has become a practical part of a gastro-intestinal examination.

The question as to what percentage of gall-stones may be shown by x-ray depends to a great extent on the quality of the films. Although the first films of the gall-bladder area may definitely show the presence in this region of one or more shadows, additional films with varying degrees of penetration should be made in order to visualize the greatest possible number of stones. In our own Clinic a survey of the histories of all operations on the gall-bladder during three years has shown that in 67 per cent. of all cases in which gall-stones were found after previous radiographic examination had been made the stones had been definitely shown on the films.

Single stones often have to be differentiated from urinary calculi. This differentiation may be established in several ways In a film of the kidney, made with the patient lying on his back and with the usual kidney compression, a gall-stone

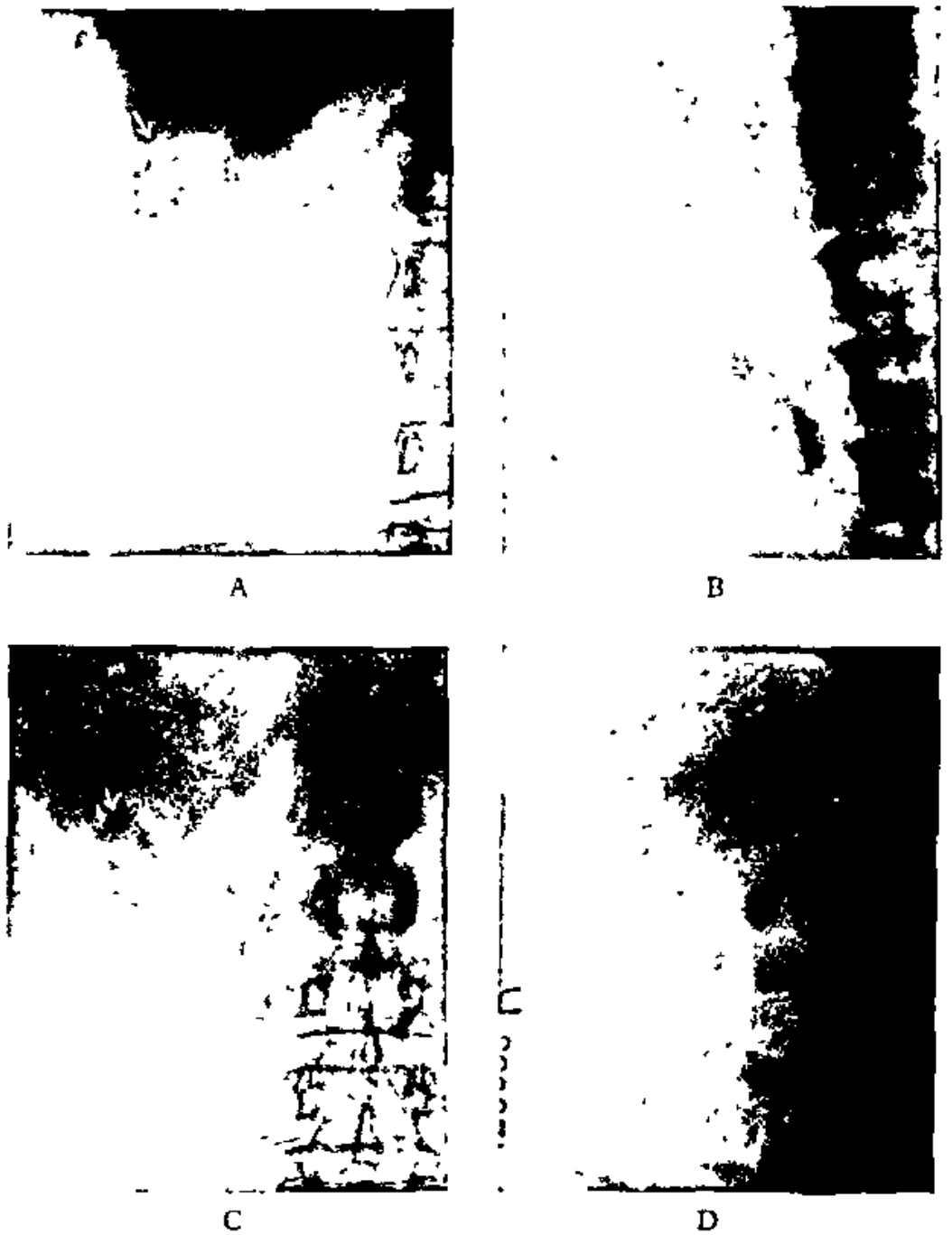
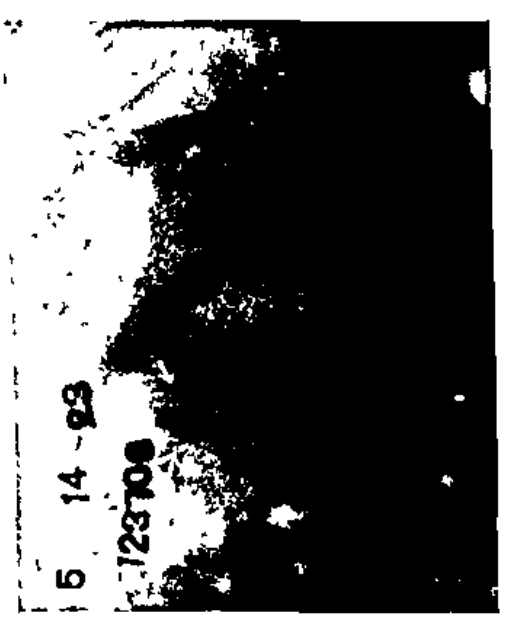


Fig. 330.—Differentiation of gall-stones from urinary calculi in two cases. First case, A and B, second case, C and D. A and C, Films taken in anteroposterior position, showing apparent displacement of stone outward and upward. B and D, Films taken in postero-anterior position, showing stone lying in a lower position and closer to spine.

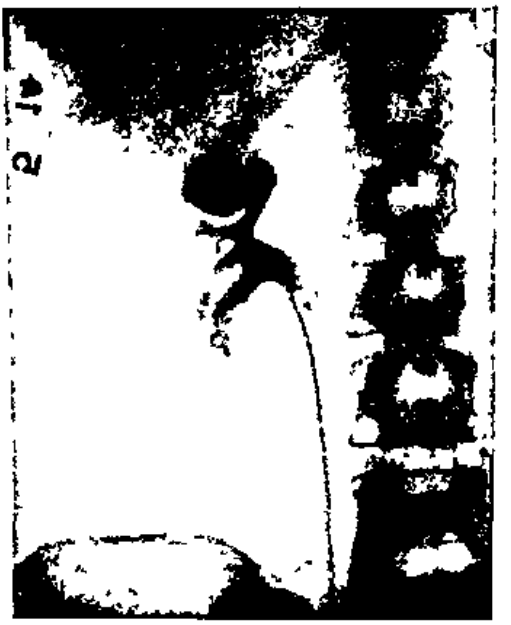
will appear large because of its distance from the plate and also because of its apparent displacement outward and upward (Fig. 330, A, C). Gall-bladder films will show a smaller shadow,

more distinct in outline, in a lower position, and lying close to the spine (Fig. 330, B, C). On the other hand, stones lying in

A



B



C

Fig. 331.—Comparison of films made in anteroposterior position, A, and postero-anterior position, B, showing little apparent change in size in stones lying in the center of the body. Differentiation made by pyelogram, C, showing localized hydronephrosis with stone.

the center of the body show little apparent change in size in a comparison of the kidney and gall-bladder films (Fig. 331, A, B);

and in the case of a stone in a gall-bladder which is firmly fixed by adhesions the comparison of the kidney and gall-bladder films show but little apparent change in position Fortunately, however, these conditions are rare

Gall-stones are usually round and show a center of lesser density, while kidney stones are more often oblong and are of even density throughout *x*-Ray films of opaque catheters passed into the right ureter, with or without injections of sodium iodid, will often identify a kidney stone or will prove the shadow to be outside of the genito-urinary tract Stereoscopic films of

Fig 332.—Calcified retroperitoneal glands

the kidney, which are made routinely in urinary examinations, will often determine the source of the suspicious shadow to be a kidney calculus if it lies close to the back, or a gall-stone if it lies closer to the abdominal wall Lateral films of the upper abdomen may also determine the position of a shadow in its relation to the kidney or gall-bladder area, but as it is generally impossible to get gall-stone shadows on lateral plates, films taken with the patient in both the anteroposterior and postero-anterior positions are the most useful.

A group of small urinary calculi in the kidney may closely simulate biliary calculi (Fig 331, A, B), in most instances these

may be differentiated by a pyelogram (Fig. 331, C). If the examination is repeated at a later date, a suspicious shadow, if caused by a urinary stone, may have passed to a lower point in the urinary tract, while in the case of a biliary calculus the shadow will usually occupy the same position as at the previous examination

There are other opaque substances than stone which may simulate gall-stone shadows, such as diverticula of the colon or small intestine filled with barium, enteroliths in the intes-

A B

Fig. 333 —A, Cholecystitis with gall-stones B, Same case, showing duodenal deformity caused by gall-bladder

tines, foreign bodies, and calcified glands. All except the last mentioned may usually be ruled out by a later examination after catharsis. Calcified glands show a fuzzy outline (Fig 332) unlike any gall-stone shadow, and usually this observation together with their location is sufficient for their identification In general the above-cited factors cover the differential diagnosis of biliary calculi from the standpoint of the roentgenologist.

Cases in which indirect signs of gall-bladder disease are found by x-ray examination form a very interesting group. They include deformities of the duodenum or of the duodenal

end of the stomach which may be due to pressure of a distended gall-bladder on the barium-filled digestive tract; to adhesions

Fig 334.—Duodenal deformity caused by gall-bladder

Fig 335.—Obstruction of duodenum with deformity of duodenal cap caused by pressure from distended gall-bladder

from a pathologic gall-bladder which pull across the duodenum or fix the pyloric end of the stomach, or to reflex spasm of the first portion of the duodenum, causing it to be only partially

A B

Fig. 336.—A, Gall-bladder visible because of thick wall and inspissated bile. B, Same case, showing pressure deformity of stomach caused by pathologic gall-bladder

Fig. 337.—Deformity of duodenum caused by gall-bladder adhesions. (Same case as Fig. 339)

filled during the examination. These deformities are quite characteristic in outline (Figs. 333–337). In the case of a distended gall-bladder which presents a smooth regular convexity

the pressure against the intestines or stomach produces a concave filling defect with a smooth regular outline, which cannot be eliminated by any method of examination. Adhesions fix the pyloric end of the stomach well up and to the right; or if they cause tension across the duodenum they produce an irregular filling defect which cannot be eliminated by the administration of atropin; whereas a reflex spasm of the duodenum due to an irritable gall-bladder may usually be eliminated by the administration of an antispasmodic. Adhesions to the hepatic flexure of the colon fix the colon in a definite position from which it cannot be moved under fluoroscopic examination These appearances which we have just described are indirect evidences of gall-bladder disease and should be considered as such in the final diagnosis.

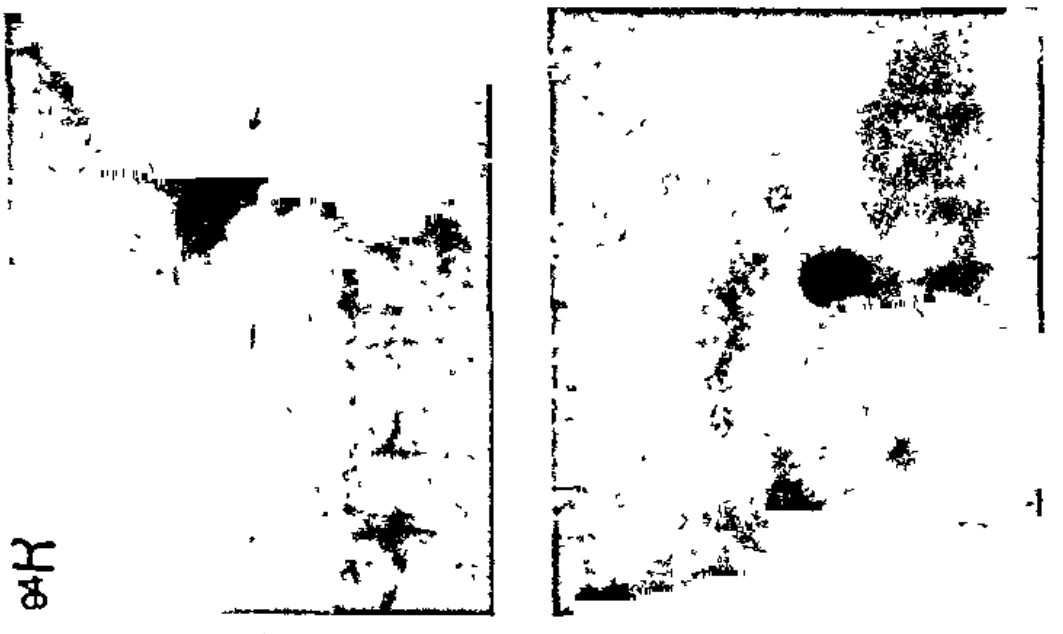
The outline of the gall-bladder may sometimes be very distinctly seen on the *x*-ray films of the gall-bladder area or on films of the gastro-intestinal tract and sometimes on kidney films We believe that this shadow is caused by a thickened wall which usually betokens a pathologic gall-bladder, especially in those cases in which the clinical symptoms indicate a cholecystitis. In such cases the *x*-ray plates often furnish the balance of evidence necessary to satisfy the surgeon that surgical intervention is indicated

It would appear that no further aid can be given by the roentgenologist in the study of patients presenting symptoms suggesting gall-bladder disease, particularly if none of the abovementioned findings can be demonstrated In such a case the roentgenologist should report that the *x*-ray examination of the gall-bladder shows no evidence of pathology, and the referring physician, bearing in mind that a percentage of cases of positive gall-bladder disease cannot be demonstrated by any of the present methods of *x*-ray examination, properly does not accept this report as ruling out the possibility of gall-bladder disease in the presence of characteristic clinical symptoms in the upper right quadrant, and on this clinical evidence he often bases a decision that an operation is indicated

Is there any further aid which the roentgenologist may offer

in such cases? The answer is suggested by the following experience: Some time ago, in a study of our statistics, we found that many patients were coming to the Clinic upon whom operations had been performed because of symptoms of gall-bladder disease. The symptoms had not been relieved, and all of these patients were suffering with intermittent pain in the upper right quadrant In many of these cases *x*-ray examination of the right kidney after the injection of sodium iodid showed a hydronephrosis. Further study showed that 30 per cent. of all our cases of hydronephrosis of the right kidney had been operated upon for either appendicitis or gall-bladder disease. Among 63 cases of hydronephrosis, *x*-ray examination showed that in 40 cases (about 63 per cent.) the lesion was on the right side This experience has made us realize the importance of investigating the right kidney in cases of suspected gall-bladder disease in which no direct or indirect evidence is found after a careful *x*-ray examination.

We are convinced that by these methods which I have outlined, together with a consideration of the clinical history and symptoms, a correct diagnosis of disease of the gall-bladder can be made in the great majority of cases.



A B

Fig 338.—A, A large gall-bladder filled with calculi B, *x*-Ray of same case after barium meal, showing relation of gall-bladder to stomach.

Fig 339 —*x*-Ray of case in which operation revealed a very small contracted tube-like gall bladder containing many stones

Fig 340 —*x*-Ray of case in which operation revealed a thickened gall-bladder with two large and three or four smaller stones

Fig 341 —Stone in gall-bladder area The possibility that this was a kidney stone was ruled out by a pyelogram

Fig 342 —Large gall-bladder containing stones

Fig. 343.—x-Ray of case in which operation revealed an enlarged gall-bladder containing stone.

Fig. 344.—x-Ray of case in which operation revealed a gall-bladder of natural size and shape containing many small irregular stones.

Fig. 345.—x-Ray of case in which operation revealed a small gall-bladder containing four or five small stones

Fig. 346.—x-Ray of case in which operation revealed a gall-bladder containing one large and one small stone.

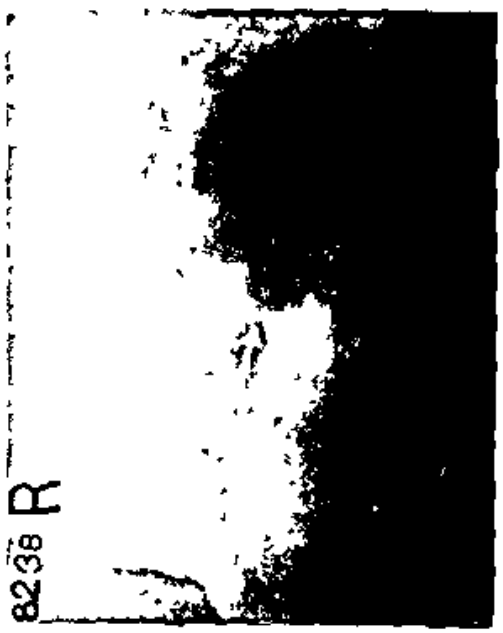


Fig 347 —x-Ray of case in which operation revealed a gall-bladder containing fifty stones, the largest the size of a 5-cent piece

Fig 348 —x-Ray of case in which operation revealed one large rough olive-shaped stone

Fig 349 —x Ray of case in which operation revealed a slightly enlarged gall-bladder filled with stones.

Fig 350 —Gall-bladder containing at least one large stone

Fig 351 —x-Ray of case in which operation revealed an enlarged gall-bladder filled with a large number of small stones

Fig 352 —Small gall-bladder containing many stones

Fig 353 —Small gall-bladder containing many stones.

Fig 354 —x-Ray of case in which operation revealed a rather long gall-bladder filled with many small stones

Fig 355.—x-Ray showing one large stone in gall-bladder area

Fig 356.—Gall-bladder film showing six large stone shadows

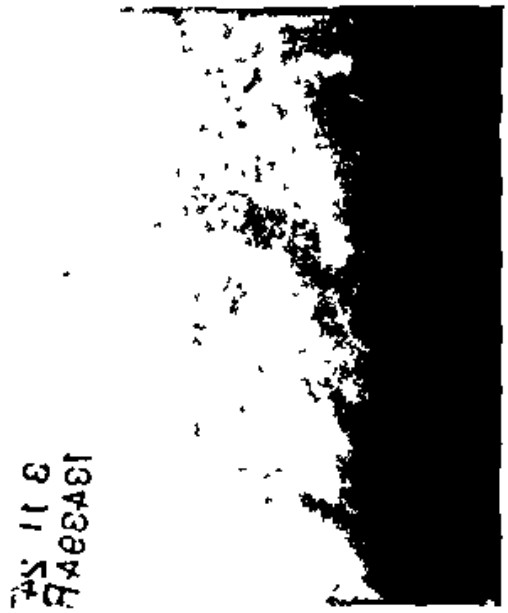


Fig. 357.—Large gall-bladder containing many small stones

Fig 358.—x-Ray of case in which operation revealed an enlarged gall-bladder with greatly thickened wall containing one large stone.

Fig. 359.—A large gall-bladder which may or may not contain stones (Case was not operated.)

and ample space for laboratories. In the basement are the radium emanation plant, the physics laboratory, and the x-ray transformers The radium emanation plant, designed in accordance with the work of Duane, was made in our mechanical department By means of this emanation plant 400 millicuries of radium emanation are made available daily from 1 gram of radium in solution The safe containing the radium in solution

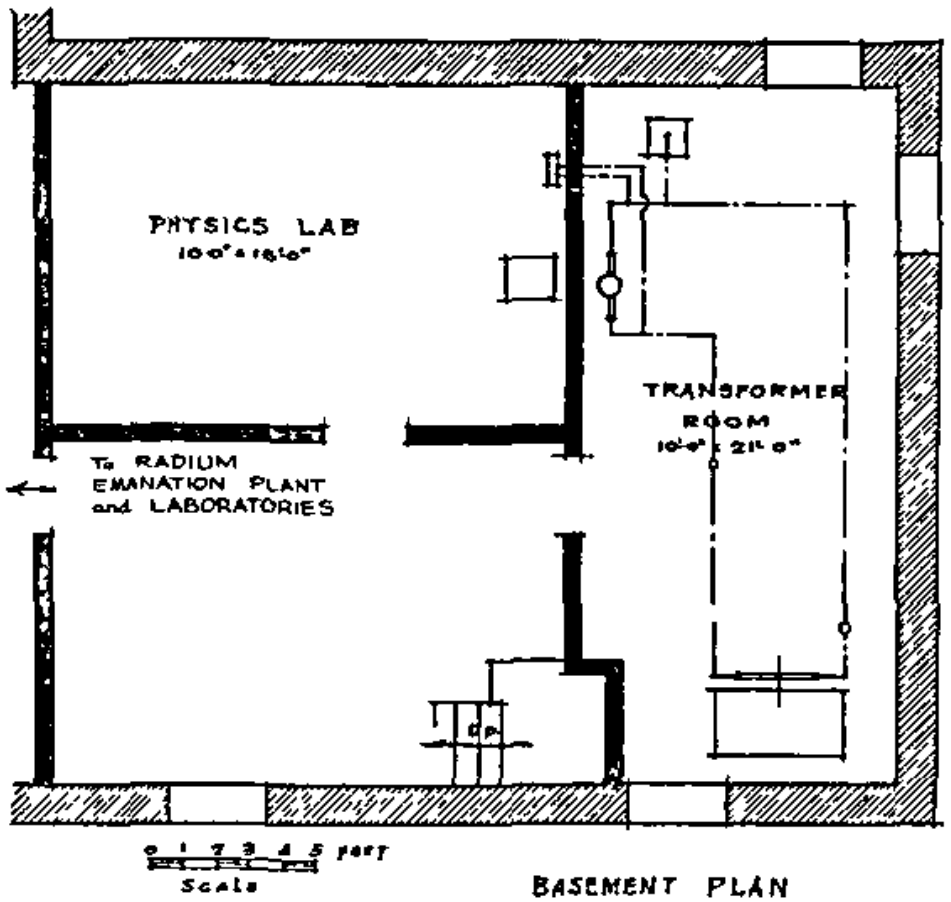


Fig 360 —Specialized hospital for radiation therapy Floor plan of basement

is located in a vault of solid reinforced concrete with walls 18 inches thick The conducting glass tubing penetrates the walls to two series of mercury vacuum pumps, so that the operator is exposed to a minimum amount of emanation

The fact that the x-ray transformer and a large part of the conducting copper tubing is located in the basement (Figs 360, 361) obviates any danger to the patient in the treatment room above from high-tension wiring This arrangement also pro-

tects the patient from more than a minimum amount of noise and odor. A lead from the wiring of the treatment transformer into the Physics Laboratory makes possible readings of intensity, potential and other working factors under practical working conditions or during a treatment.

On the first floor are the reception room, wards, and lavatories, an office, examining rooms, and the treatment room. On the second floor are wards, lavatories, storage space, and the

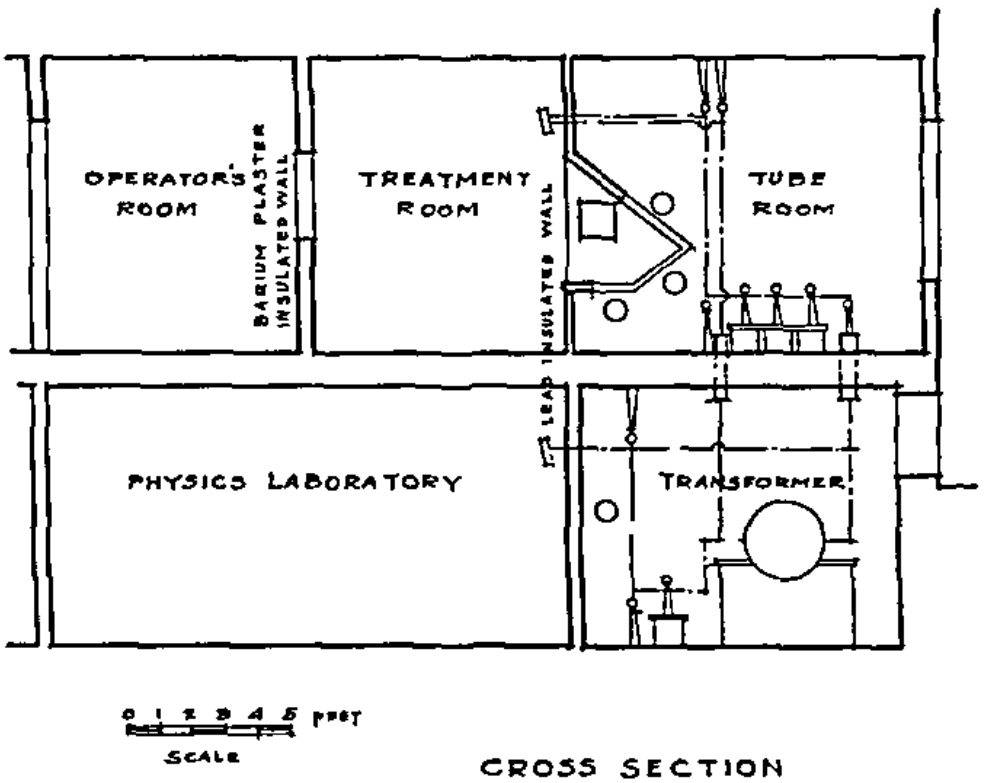


Fig. 361.—Specialized hospital for radiation therapy. Cross-section through basement and first floor, note position of transformers directly beneath the tube room, leading to laboratory

kitchen, and on the third floor is a laboratory for the physical investigation of radium.

The sketches and photographs (Figs. 362, 363) show in a general way the arrangement of the treatment unit, which consists of an observation room and a treatment room. In the observation room (Fig. 364) are the controls of the transformer and an inclined table on which are six controls for the six Coolidge tubes around the treatment couches. The walls of both treatment and observation rooms consist of 3 inches of barium sul-

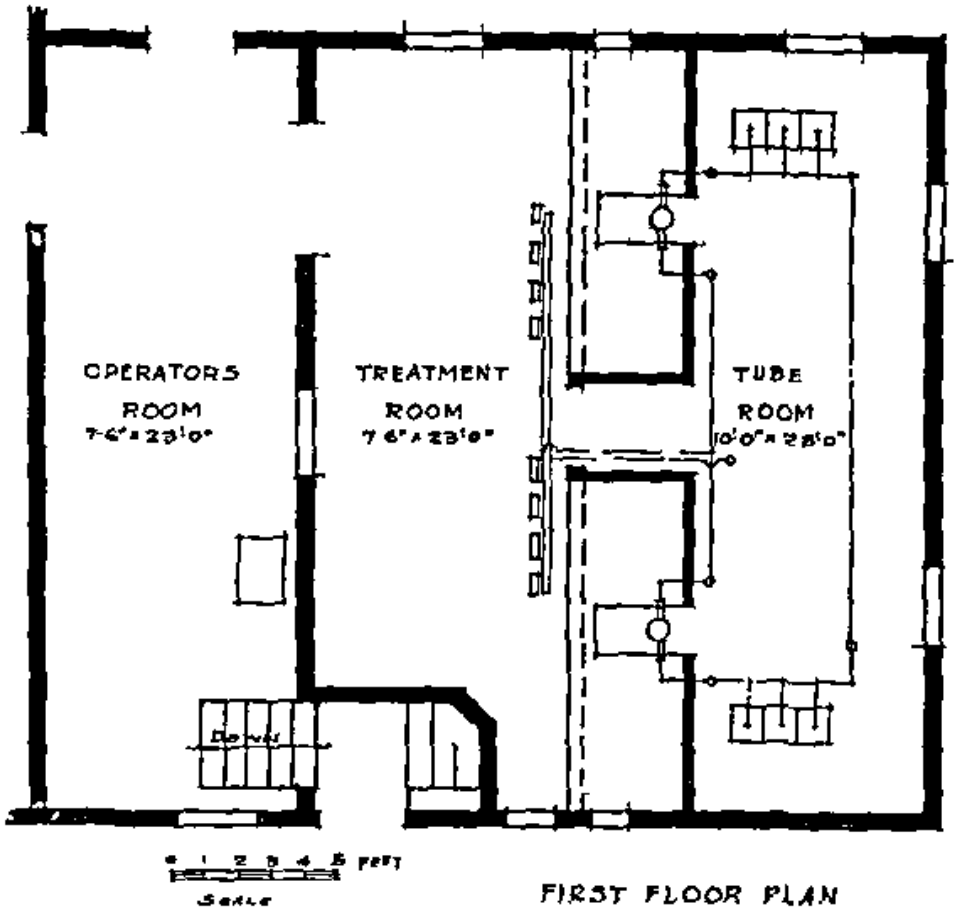


Fig. 362.—Specialized hospital for radiation therapy. First floor plan.

Fig. 363.—Specialized hospital for radiation therapy. Treatment couches as seen from operator's room, showing door into tube room.

phate incorporated in plaster upon metal laths. Directly over the control board is a lead glass window through which the patients under treatment can be observed. The only high-tension wiring in the treatment room are the two leads to a bank of milliammeters (Fig. 365), 1 meter for each of the six Coolidge tubes, and one master meter whereby the total milliamperage of the tubes in use during a treatment may be read. There are

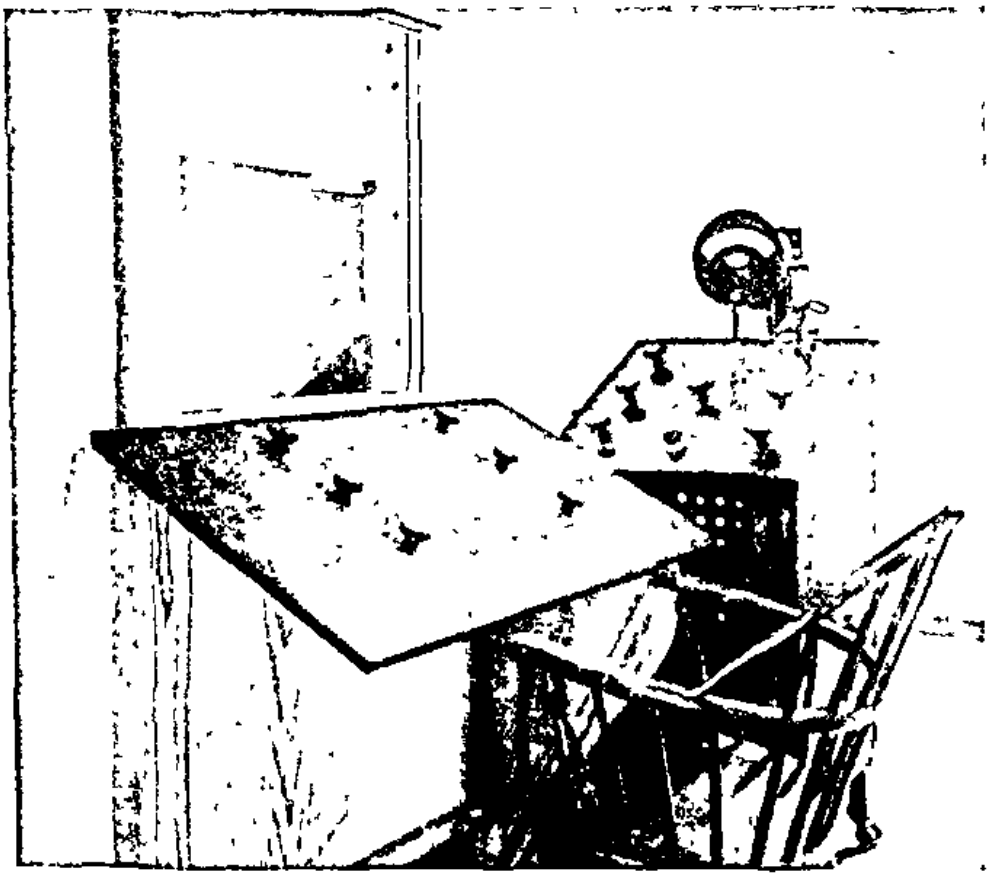


Fig. 364.—Specialized hospital for radiation therapy. Operator's control board, with windows giving view of treatment couches.

two couches (see Fig. 363) which permit the simultaneous treatment of two similar cases, each by one, two, or three tubes, as may be desired. Each of the two couches consists of a wooden framework supporting a sheet of lead $\frac{1}{4}$ inch in thickness, and all the walls around the treatment couches are lined with $\frac{1}{4}$ inch of lead. This gives complete protection from direct rays, so that one may enter the treatment room without danger. All the apparatus necessary for the direct administration of the radiation

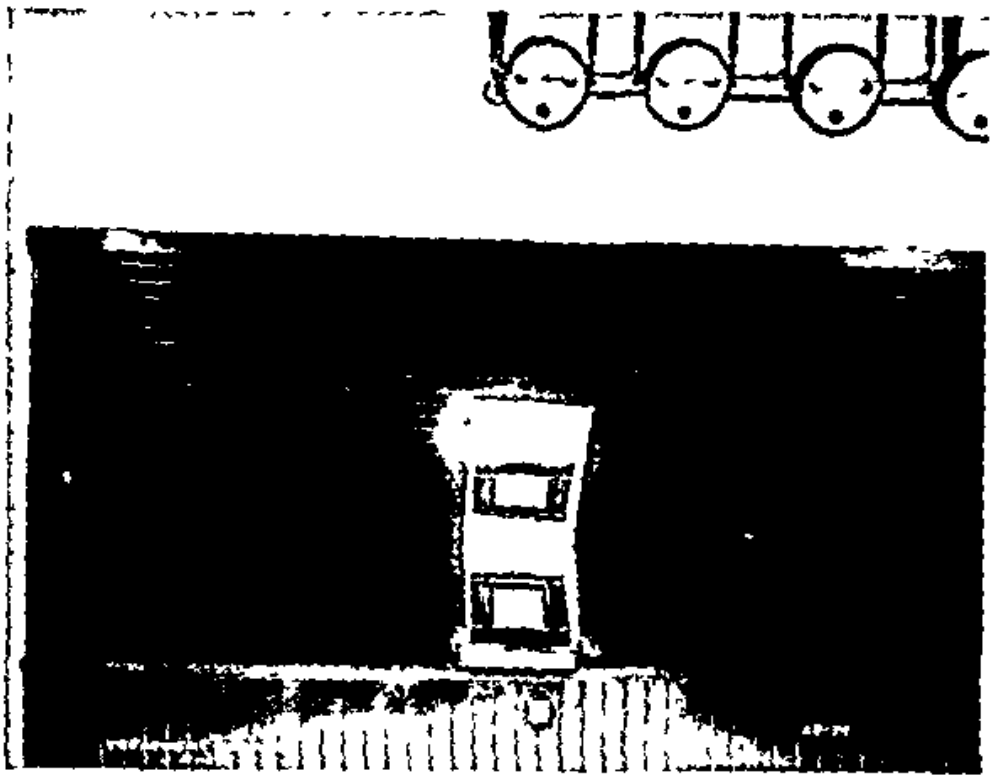


Fig 365.—Specialized hospital for radiation therapy Treatment couch showing portals of entry for treatment and part of bank of milliammeters

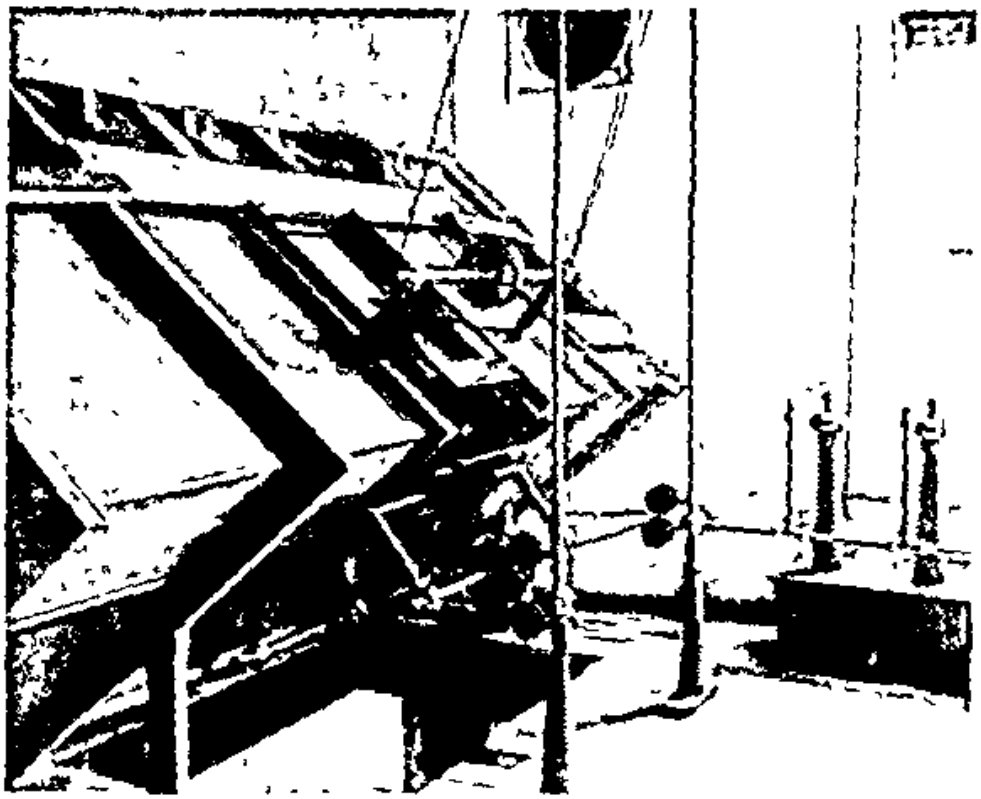


Fig 366.—Specialized hospital for radiation therapy Tube room, showing back of treatment couch, with tubes in position for treatment

—the Coolidge transformers and the necessary high-tension wiring—is contained in a room back of the treatment room (Fig. 366), thus obviating the effect on the patient of the sight of complicated and dangerous appearing apparatus. A door from the treatment room gives access to this room for the necessary adjustment of tubes and filters. Portals of entry are

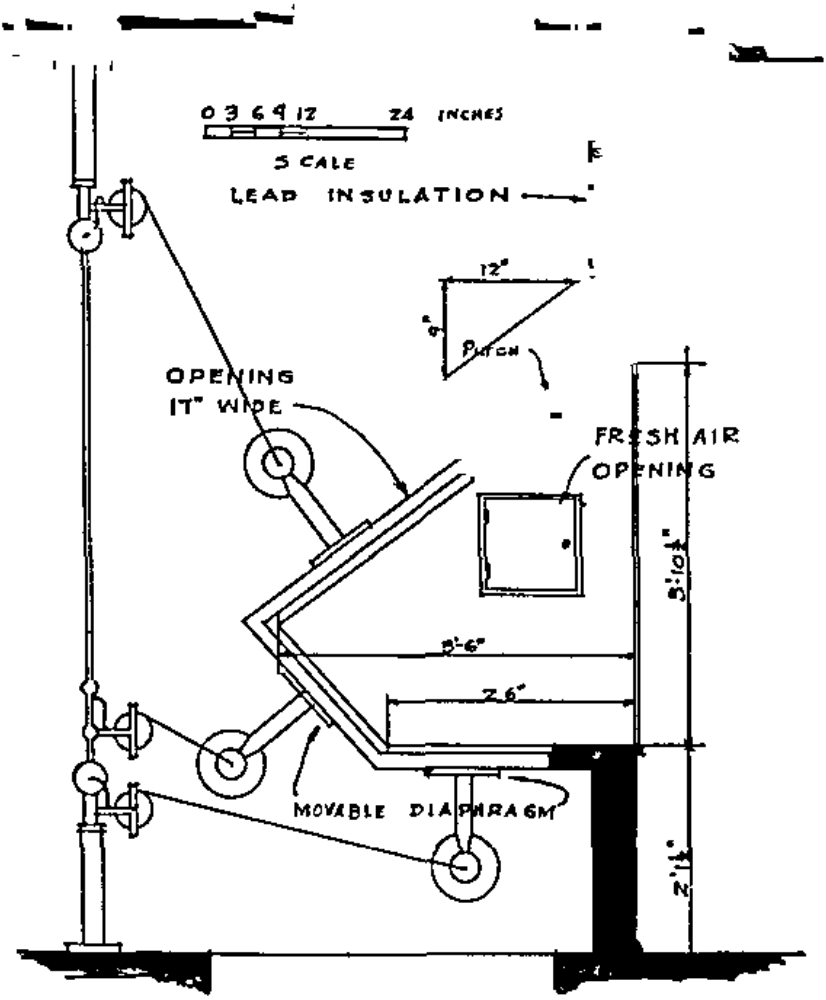


Fig 367.—Specialized hospital for radiation therapy. Cross-section of treatment couch and tube room.

cut through the walls of the couches, which are arranged at angles as shown in the diagram (Fig. 367), the degree of the angle having been determined by the average cross-section of the human body. As the *x*-ray tubes are on slides, any area of the body may be radiated. Figure 367, which shows the back of the couch with three tubes in position, gives an idea of the way in which the radiation from each tube may be directed through a

portal of entry These rooms are thoroughly ventilated by suction fans, and few of our patients have suffered from nausea or malaise for more than a few hours.

This arrangement has several advantages:

1. Two patients may be treated simultaneously under the same conditions, and by directing the radiation through several portals of entry at the same time the total time for treatment is reduced by at least one-half.

2 The patient lies comfortably upon a mattress and is not distressed by the sight of complicated apparatus.

3. The patients and the operator are entirely surrounded by $\frac{1}{4}$ inch of lead and no high-tension wiring endangers the patient

4 The arrangement of the side walls of the treatment couches makes it possible to vary the direction of the radiation to an extent that is impossible with right-angled walls

In addition to the constant co-operation with the department of biophysics in the determination and regulation of the dosage, and the investigation of the effects of radiation upon normal and pathologic tissues, we are indebted to Hugo Fricke, Ph D , for the electroscope and the ionization chamber designed by him, and to Mr Seitz, of the electromechanical department, for their manufacture

A brief word regarding the method of application of radiation to the individual case and regarding our present point of view as to the types of cases suitable for radiation may be of interest

After considerable investigation in collaboration with the department of biophysics we came to the conclusion that it would be impossible by deep *x*-rays alone to administer a therapeutic dose of radiation to such deep-seated lesions as carcinoma of the uterus or carcinoma of the rectum. Fortunately, however, in any case in which radiation is therapeutically insufficient radium can be employed to supply the percentage of the required dose that is lacking. Even with the small quantities of radium ordinarily available it is possible to administer a therapeutic dose of radiation if the radium and *x*-ray intensity

curves are understood and properly applied. By superimposing radium intensity curves over *x*-ray intensity curves, through the necessary portals of entry we are able to build up an evenly distributed and homogeneous therapeutic dose of radiation not only to the tumor itself but also to neighboring areas that may or may not be malignant. Thus we approach the technic of the surgeon who has learned the necessity not only of removing malignant tumors but also of making a wide-spread dissection.

To determine the correct dosage for each individual case we use the method of Dessauer. A lead wire is placed about the body of the patient at the site of the lesion to give the configuration of the body. After making measurements to determine the exact site of the lesion to be treated a cross-section of the patient is made and the preferred method of approach through various portals plotted. By this method we are able to determine with reasonable accuracy the amount of radiation to reach all points within the cross-section of the body. In a given case we attempt to administer the radiation treatment within one week or ten days. Either radium or *x*-rays or both are used first, according to the convenience of the operator.

It is impossible at this early date to make any statements as to positive cures, but we can say with certainty that certain malignant growths yield readily to proper radiation therapy, and that patients with tumors of these types seem to convalesce more rapidly after the application of the combined method of therapy than after surgery. We do not treat all malignant cases by radiation alone, but the closest possible co-operation is maintained between the radiologist and the surgeon in the attempt to determine the preferred method of treatment in each particular case, *i. e.*, whether surgery or a combination of surgery and radiation will give the most satisfactory results.

The solution of many of the problems of radiation therapy must be provided by the biophysicist, who must give us more information regarding the biologic reactions of cells under varying conditions The physical laws governing radium and the *x*-rays are fairly well understood, but the biologic problems involved in their application have hardly been approached.

JOHN TUCKER

DEPARTMENT OF INTERNAL MEDICINE

AN UNUSUAL CASE OF BANTI'S DISEASE WITH EVIDENT RECOVERY FOLLOWING SPLENECTOMY

WITHIN the last few years, experience has shown that about 75 per cent. of the cases of Banti's disease in which a splenectomy is performed recover from the operation. It is advisable, therefore, that, once the diagnosis has been established, the spleen be removed at the earliest possible moment, provided the operation is justified by the condition of the patient. Although without operation the patient may live for many years in a fair or indifferent condition of health, the probability of cure by any other means is extremely doubtful because of the blood destruction which is undoubtedly due to some influence exerted by the pathologic spleen. A most striking instance of the value of splenectomy in an apparently hopeless case is shown by the case reported below, which presented the following unusual features.

1. The probable duration of the disease for more than twenty years

2. The presence of marked anemia, anasarca, and myocardial incompetency, making the patient an extremely poor surgical risk.

3. An almost unbelievable recovery in spite of several major surgical procedures which became necessary subsequent to the splenectomy.

Case Report.—The patient, a young man twenty-six years of age, presented himself at the Cleveland Clinic for examination in January, 1923. He complained of extreme weakness, pallor, and swelling of the body. There was no family history of anemia,

chronic hemorrhages, or chronic illness The patient had been married for two years, his wife was living and well and had had no pregnancies The patient had had pneumonia at the age of two and a half years, tonsillitis at the age of sixteen, and two and a half years before he came to the Clinic he had had an illness which lasted for several weeks This illness was called malaria, although there were no chills and only slight fever, and no blood studies were made

The present illness dated from the attack of pneumonia at two and a half years of age. Shortly afterward the patient's mother had noticed a gradually increasing pallor, with "jaundiced" eyes The patient also began to have periodic "bilious" spells during which his skin had a yellow tinge and the urine was dark colored The stools seemed to be normal in appearance He was troubled with frequent attacks of "nosebleed," but a cut in the skin would heal promptly

As his condition bordered upon chronic invalidism, the patient was almost constantly weak and pale until the age of eighteen years, when he was suddenly seized with severe cramps in the upper abdomen, and an infected gall-bladder containing 6 stones was removed This operation relieved the colic, but did not lessen the pallor or produce any increase in strength In August, 1920 the patient went to Oklahoma and remained there for three years, without improvement A complete physical examination—the first that had been made—prior to the gall-bladder operation showed an enlarged spleen

About three years before he came to the Clinic the pallor of the skin and lips was definitely increased and the urine became constantly dark in color There were no tarry stools, no subcutaneous hemorrhages or loss of blood except for an occasional attack of epistaxis

Three weeks before coming to the Clinic the patient noticed the gradual onset of shortness of breath associated with a hacking cough His lower extremities began to swell, his pallor increased, and he was unable to sleep except when propped up in bed He had no headache, and aside from the weakness and air-hunger no other discomfort His appetite was fairly good,

but the bowels were quite costive. For about a week the urine had been red in color.

Physical examination showed the patient to be a well-developed though slim and rather poorly nourished young man of twenty-six years of age. The skin was a light lemon yellow in color with a marked underlying pallor; no petechiæ were present. The pupillary reactions were normal, but the sclera appeared slightly icteric. A dental examination showed all teeth vital except an incisor which, while non-vital, revealed no *x*-ray evidence of apical pathology. The tonsils were atrophic and no abnormal enlargement of lymph-glands was found.

The contour and expansibility of the chest were normal except for a slight lagging of the median half of the costal margin. No abnormal findings could be demonstrated in the lungs. The heart was moderately enlarged and a systolic thrill was palpable over the precordium, with a hemic murmur at the base and a continuous venous hum audible over the jugular bulb. Palpation of the pulse showed a rapid rise and fall—rate 90, blood-pressure 105/60, temperature 99 2° F.

The abdomen was rounded and slightly protuberant, especially in the left hypochondrium The spleen was enlarged, extending about three fingerbreadths below the left costal margin and moving downward on inspiration. It was firm in consistency, apparently quite freely movable, and the surface and edge were smooth No enlargement of the liver could be demonstrated by either palpation or percussion There was no ascites The genitalia were normal and rectal examination revealed no hemorrhoids or other abnormality. The ankles were edematous and the subcutaneous tissues of the lower extremities felt full and tense. The patellar and Achilles' reflexes were equal and active.

Clinical laboratory findings were as follows:

Urine Examination.—Acid reaction; specific gravity 1012; albumin ++; sugar negative; benzidin positive; bile pigment very slight trace; urobilin negative. Microscopic examination showed the urine loaded with red blood-cells; 15 to 20 white blood-cells per high-power field; and a few finely granular casts

Blood-counts.—Red blood-cells, 1,420,000, white blood-cells, 6600, hemoglobin, 29 per cent (Dare), Color index, 1 Differential count (200 cells counted)· Polymorphonuclears, 58 per cent., eosinophils, 2 per cent , basophils, 1 per cent ; small lymphocytes, 39 per cent., character of red blood-cells—anisocytosis with few megalocytes and microcytes, no myelocytes or nucleated red blood-cells

Blood Chemistry (per 100 c c) —Sugar, 113 mg., urea, 18 mg ; uric acid, 3 8 mg , chlorids, 645 mg , bile pigment positive, Wassermann 0-0-0, Blood-Group IV Unfortunately no preoperative blood-count was made.

Stool Examination —Color normal, parasitic ova negative; occult blood negative

On account of the serious myocardial incompetency a gastric analysis was not attempted

Diagnosis.—(1) Banti's disease, (2) acute nephritis without hypertension.

Treatment.—A blood transfusion was performed on February 26, 1923, using a Group IV donor The patient promptly hemolyzed the foreign blood, with the usual febrile reaction On the following day the blood-count showed a slight increase in the red blood-cells, viz , 1,700,000 At this time the patient refused to submit to a splenectomy. He remained at home for two months, during which time the dyspnea and the swelling of the legs gradually increased. He became orthopneic and slightly cyanosed Digitalis derivatives, together with iron and arsenic by mouth or hypodermic, produced only slight improvement

A month and a half later the red blood-cell count had fallen to 1,100,000, and in view of the alarming condition of the patient his family gave full consent to the removal of the spleen. The patient's blood was matched directly with that of the donor, and two transfusions were given before operation An unsuccessful attempt was made to secure better cardiac compensation by the use of digitalis In view of the almost hopeless outlook, however, we felt justified in risking the operation, and a splenectomy was performed on April 25th. There was no post-

operative shock and very little loss of blood. The patient remained orthopneic, but the lips and fingers acquired a pinkish hue. Ten days after the operation, during a fit of coughing, the wound, which was not healing well, broke open, with resultant protrusion of the omentum and some of the small intestine. A secondary closure was made and, although we fully expected it, peritonitis did not develop However, a partial intestinal obstruction with constipation and frequent vomiting did develop Fluid was given per rectum and by infusion, but the emesis of gastric contents continued.

A week later, in the hope of giving relief, the incision was reopened, and a small amount of pus was found extending down to the peritoneum A presenting bit of small intestine was sutured to the abdominal wall and an enterostomy performed Feedings were given into the distal gut and the vomiting ceased shortly afterward. The patient improved rapidly, although he suffered considerably from pancreatic digestion of the skin in spite of the use of mutton tallow.

Eleven days afterward (on May 23d) under local anesthesia, an attempt was made to close the enterostomy opening by inversion of the mucosa and by freeing the intestine from the abdominal wall. The incision was packed with iodoform gauze, but a seepage of chyme resulted. A second effort was made to close the fistula on June 18th, but the closure was effective for only a few days.

The sixth and last major operative procedure was performed on June 24th, just two months after the splenectomy. The old area of incision was reopened, the fistulous portion of the intestine resected, and the gut joined by an end-to-end anastomosis.

A final blood transfusion, given eleven days later, closed the surgical program.

The pathologic examination of the spleen revealed the usual fibrosis which occurs in Banti's disease with an accompanying chronic passive congestion.

The patient's general condition remained amazingly good throughout these unfortunate complications. His dyspnea

Blood-counts.—Red blood-cells, 1,420,000; white blood-cells, 6600, hemoglobin, 29 per cent. (Dare); Color index, 1 Differential count (200 cells counted). Polymorphonuclears, 58 per cent ; eosinophils, 2 per cent ; basophils, 1 per cent , small lymphocytes, 39 per cent., character of red blood-cells—anisocytosis with few megalocytes and microcytes, no myelocytes or nucleated red blood-cells.

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Therefore, if we accept the observations of the parents, we are confronted with the very unusual condition of a prolonged chronic splenic anemia without cirrhosis of the liver, ascites, or gastric hemorrhages. Banti, in his classical description of the disease, included in the syndrome anemia, splenic enlargement, cirrhosis of the liver, ascites, and a tendency to hemorrhages, especially gastric. We believe that he was describing the end-stage of this disease, and that he included in his classification anemias with enlarged spleen, such as Gaucher's disease. In our case, with the extreme anemia and cardiac incompetency, we would probably not have attempted splenectomy had hepatic cirrhosis with ascites been present. However, Dr. Charles H. Mayo has reported some instances of recovery from splenectomy even in the presence of cirrhosis.

We would call attention also to the leukocytosis following operation and the gradual disappearance of hematuria subsequent to the splenectomy

In the preoperative consideration of the differential diagnosis we considered primary anemia, Gaucher's disease, and hemolytic splenic anemia (Minkowsky). We believed that primary anemia was ruled out by the long duration of the symptoms, the absence of any evidence of a subacute combined sclerosis of the spinal cord, even though the disease had existed for years, and the blood-picture We could not absolutely rule out Gaucher's disease in our preoperative diagnosis, but we did not regard this as probable since in such a disease the spleen is usually much larger. There was no history of familial anemia to suggest congenital hemolytic jaundice.

The subsequent history of this case together with the pathologic findings in the spleen were sufficient to justify our diagnosis of Banti's disease.

SUMMARY

1. This case of Banti's disease had probably existed for over twenty-three years, during which time change of climate, rest, and drugs were used to no avail.

2. Almost complete recovery has taken place since the removal of the spleen, even though before operation the patient

was suffering from very severe anemia and myocardial insufficiency.

3 The patient revealed a remarkable power of recovery in spite of several postoperative mishaps requiring six consecutive surgical procedures

4. Splenectomy should be advised for Banti's disease even though the condition may have been chronic for several years, and the patient's physical condition is regarded as critical. The patient should be given the chance of recovery by means of the one effective method of cure.

JUSTIN M. WAUGH

DEPARTMENT OF OTOLARYNGOLOGY

REPORT OF A CASE OF AN UNUSUAL FOREIGN BODY IN THE ESOPHAGUS

THE case herewith reported is that of a child eight years old who swallowed a machine bobbin about four days before admission to the Cleveland Clinic. The bobbin, which was of the ordinary kind used in sewing machines, consisting of two flanges $\frac{7}{8}$ inch in diameter connected by a hollow post $\frac{5}{16}$ inch in length (Fig. 368), had been given him by a sister to hold, and in his

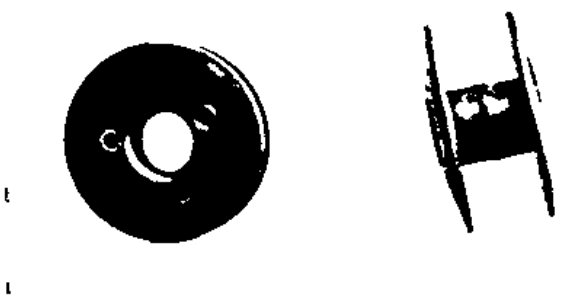

FIG. 368.—Machine bobbin swallowed by patient.

play he put it in his mouth, started to run, and swallowed it. A short period of choking and dyspnea was followed by coughing and expectoration of mucus and some substernal pain.

Various measures for the removal of the bobbin suggested by the neighbors were tried without success. *x*-Ray plates were taken in the city in which the child lived, and a very exact description of the foreign body and its location in the esophagus was sent to the Clinic with him. *x*-Ray plates taken here showed that the foreign body had not changed its position in the interval between the first *x*-ray and his admission to the

Clinic. It was impacted in the esophagus at a point about opposite the third dorsal vertebra (Figs. 369, 370).

Fig. 369.—Anterior view of bobbin lodged in esophagus

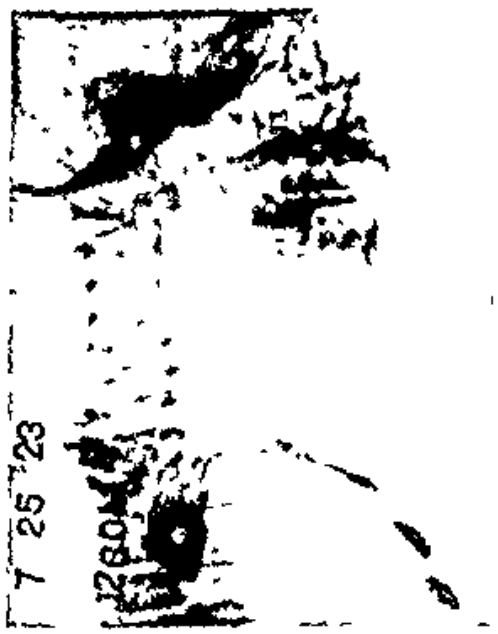

Fig. 370.—Lateral view of bobbin lodged in esophagus

The child was put to bed and all food prohibited. A preliminary examination of the esophagus was made the next day, with the following findings: The mucous membrane was quite edematous and had almost completely covered the edges of the

flanges of the bobbin. A mass consisting of food and barium which had been given at the time of the *x*-ray examination covered what was probably the post of the bobbin. The edges of both flanges could be seen for about ¼ inch, but the bobbin could not be removed in either direction, as it was so impacted that at each attempt to grasp it the forceps slipped from the edge of the flange. The child was returned to bed and the problem taken up in the laboratory.

Unlike an ordinary disk, this foreign body was stretching the esophagus in all diameters, so that during its removal there would be danger either that the upper flange would injure the partition between the esophagus and the trachea or that the lower flange would wound the esophageal wall. In the former

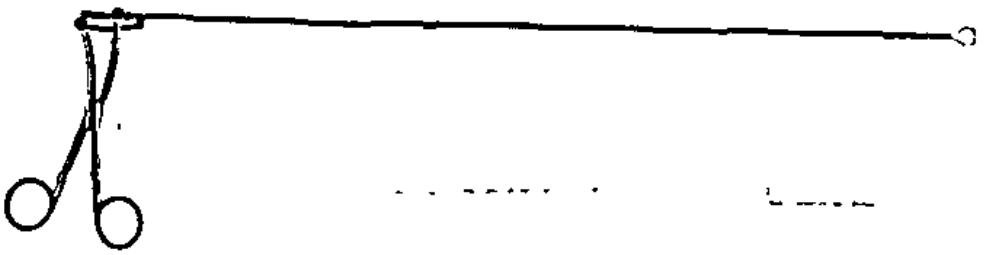

Fig 371.—Adaptation of Jackson rotation forceps for removal of bobbin.

case a tracheo-esophageal fistula would result and in the latter a mediastinitis

The ordinary Jackson rotation forceps were ideally constructed for removing the bobbin, but did not open wide enough to grasp the post. The temper was, therefore, taken out of the tip of the rotation forceps and the curvature of the end modified so that just enough distance intervened between the extreme ends of the lips of the grasping tips partially to encircle the post (Fig. 371). Although it was not possible to make the distance between the two ends sufficiently great to encircle the post completely and to tighten them afterward, it was found that by producing direct pressure against the post with the tips somewhat closer together, these ends would spring about the post, after which they could be locked by the handle of the grasping instrument. Once having grasped the post of the

bobbin with this instrument, the bobbin could slip over any plane that offered resistance, thus greatly diminishing the danger of rupturing the esophagus by violence.

Two days later the child was re-examined under an anesthetic and the bobbin removed. The operation was followed by a slight rise of temperature, which subsided in forty-eight hours, when the child was discharged from the hospital. When he was brought to the Clinic six months later it was reported that no discomfort of any kind had followed the operation.

J. P. ANDERSON

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ARTIFICIAL PNEUMOTHORAX IN PULMONARY TUBERCULOSIS

THE 2 cases reported below illustrate important points in the treatment of pulmonary tuberculosis by artificial pneumothorax:

Case I.—On April 29, 1924 the patient, a man forty-six years of age, reported at the Cleveland Clinic for examination, complaining of fever, anorexia, and a few night-sweats, which had persisted since the development of a cold in January, and, in addition, the more recent development of occasional hemoptysis. These symptoms had been unaccompanied by any loss in weight. The patient was married, but had no children There was no history of tuberculosis in the family and no history of any previous illnesses.

Physical examination showed a well-developed and well-nourished man with a temperature of 99 6° F., pulse 90, blood-pressure 120/80 The only abnormal findings were in the right side of the chest, which revealed an impaired resonance at the right apex, increased tactile fremitus, increased vocal resonance and numerous râles, but no definite signs of the presence of a cavity. No abnormal signs were found in the left lung. *x*-Ray plates of the chest showed infiltration in the upper fourth of the right lung, with a cavity in the subclavicular area (Fig. 372, A). As the left lung was clear and the sputum positive, a pneumothorax was initiated on May 3, 1924, using the apparatus shown in Fig 373, and a needle the bevel of which was very short in order to avoid puncturing the lung. The initial pressure was —40—25 mm. of water, as read from one side of the manometer, 200 c c. of filtered air was aspirated and another 100 c c. introduced under slight pressure by altering the water levels in the bottles, the pressure being left at —25—10 mm. Two days later a refill was made, using the same apparatus except for an ordinary 18 gage needle with a short bevel. With the reading at —32—17 mm. 400 c c. of air was introduced, leaving pressures at —27—3 mm.

On May 9, 1924 another refill was made, with a reading of —20—10 mm.; 800 c c of air were introduced, leaving the pressures at 14+7 mm. This rather large refill caused some anorexia and pain in the chest, so that since that time at each refill about 400–600 c c. have been given, and the pressures left at about 10+3 (Fig 372, B).

After the initial induction the temperature became normal and has remained so, the cough has been reduced to only two attacks daily, and after

A B C

Fig. 372 —Radiographs of case of unilateral pulmonary tuberculosis in which pneumothorax was instituted, Case 1. A, Note moderate sized cavity in right apex B, After two refills. (Average refill amounted to 100 c.c) C, After twelve refills Note compression of lung to approximately one-half of original volume with maximum compression of diseased portion

the first few days the sputum disappeared Since the fourth refill there has been no cough at all, and the only distress has been a slight pulling sensation which is probably caused by pleural adhesions, (Fig. 372, C).

Case II.—On December 7, 1923 a young woman, twenty years of age, whose mother died of tuberculosis, came to the Clinic because of a cough associated with sputum which had persisted since the onset of a severe cold in the preceding September She had experienced no hemoptyses, night-

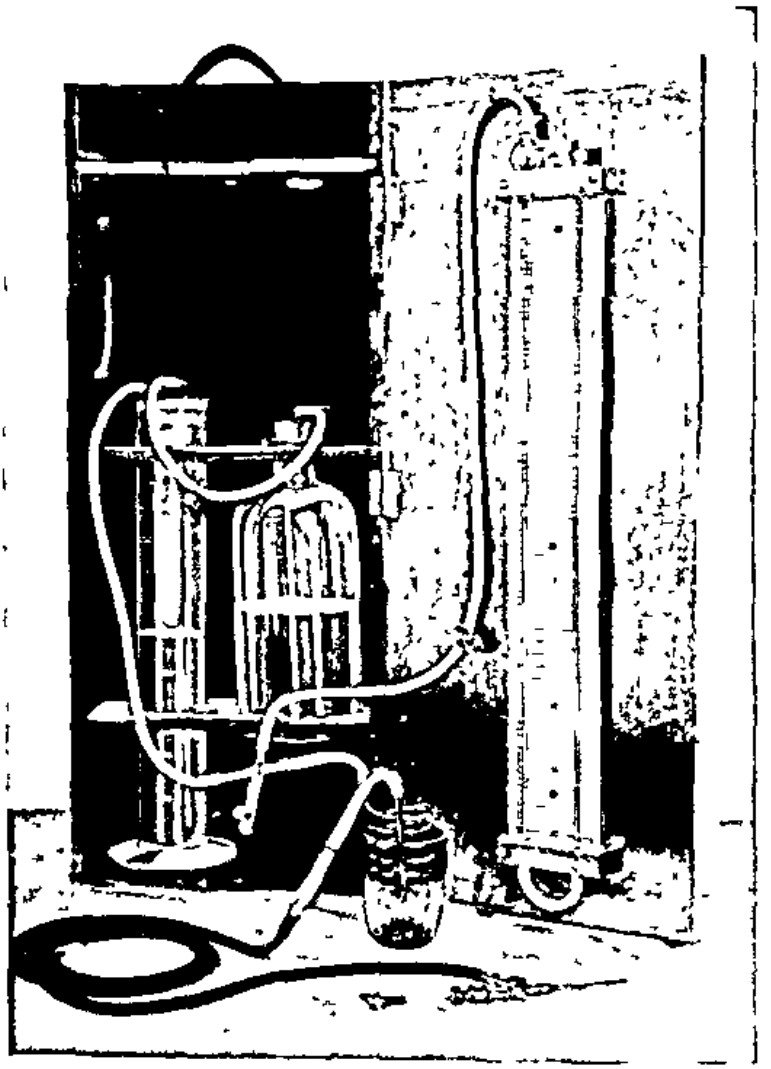

Fig 373.—Apparatus used for the induction of pneumothorax.

sweats, chills, fever, or fatigue, but there had been a loss of 7 pounds in weight during the three months since the onset of the cold.

The physical examination showed a well-developed and well-nourished young woman, 5 feet, 3 inches tall, weighing 117 pounds, the temperature was 98 8° F., pulse 96, blood-pressure 118/75. Chest examination showed diminished expansion and resonance at the right apex, with medium moist râles and an inspiratory amphoric stridor indicating a cavity which was shown on the *x*-ray film. The voice sounds were increased, but not amphoric. There were a few fine crepitations in the left lung, chiefly in the subclavicular

region The remainder of the physical examination was normal. The urine was clear The blood-count showed red blood-cells, 3,670,000; leukocytes, 77 5 per cent , eosinophils, 2 per cent , basophils, 0 5 per cent , small lymphocytes, 20 per cent The sputum contained a moderate number of tubercle bacilli.

The patient was instructed to remain absolutely at rest in bed for one month, and except when necessary to go to the bath-room, for another one and a half months *During the first three weeks mustard pastes were applied* frequently over the left apex—none over the right, at the end of five weeks of rest no abnormal physical signs could be detected in the left lung and fewer râles were present at the right apex. After two and a half months of rest *x*-ray plates of the chest showed that the lesion in the left lung had healed, but there was some doubt as to the presence of a cavity at the right apex As the physical examination showed that the coarse râles and the amphoric stridor were still present after coughing, transverse plates were made These again showed an annular shadow, thus clearing up any doubt regarding the presence of a cavity. The sputum, though small in amount, still showed tubercle bacilli As the cavity was about 3 cm in diameter, a pneumothorax was advised The fact that the lesion in the left lung had healed made this a safe procedure

DISCUSSION

Case I illustrates a case of rather advanced unilateral tuberculosis with cavitation It may be of interest to note that 2 other similar cases were examined during the same week; one was referred to the County Sanatorium, where a pneumothorax will probably be done, and the other is considering this treatment *Such cases are suitable for the immediate induction of* pneumothorax, which should not be delayed, as pleural adhesions may develop which will either interfere with or make the treatment impossible. As is shown by Fig 372 Case I had rather extensive adhesions. It should be noted, however, that in this case the greatest compression was in the region of the heaviest infiltration and the cavity was fairly well compressed.

Case II shows a far advanced lesion in one lung with incipient infiltration in the other Such cases are not suitable for pneumothorax therapy until after the infiltration in the uninfected lung has quieted down with the ordinary "rest cure" measures The pneumothorax should be done as soon as the healthy or comparatively healthy lung is well able to withstand the added strain Case II also illustrates another point, namely, that in

cases of doubt lateral plates should be made to determine whether or not annular shadows are cavities.

INDICATIONS FOR ARTIFICIAL PNEUMOTHORAX

The best test for the efficacy of any procedure is its continued use, and the use of artificial pneumothorax and its efficacy in selected cases of tuberculosis has been definitely established ever since the first reports by Forlanimi in 1895 and by Murphy in 1898 It is not a specific cure for tuberculosis, but since, by compressing the lung it causes the expulsion of much toxin-laden exudate and produces a partial or complete apposition of cavity walls, it is an exceedingly useful adjunct to the rest cure. In some cases it is possible to effect a complete cure by combining pneumothorax with the rest cure, while in others it is possible to compress a cavity sufficiently to render the sputum negative, a result of the utmost importance in cases in which a parent with tuberculosis is obliged to return home to be associated with children; in still other cases, in which there is no hope of either curing or arresting the disease, by squeezing out the caseous toxin-laden material from the lung the excessive fever, the night-sweats, and the fatigue induced by raising large amounts of sputum are controlled, and this result is, indeed, a godsend to those suffering with slowly advancing tuberculosis.

As pneumothorax is not a specific cure, it is necessary to select prospective cases with care. In the classical case of tuberculosis in which there is massive infiltration and cavitation in one lung with copious positive sputum, but minimal or no disease in the opposite lung, it is not difficult to decide regarding the advisability of a compression, but even in such a clearly suitable case it is necessary to exercise wise judgment in deciding when to induce the pneumothorax. If it be induced before the response of the patient to rest has been determined, then one may needlessly burden a patient with the inconvenience and expense of a pneumothorax when rest might have accomplished the same result. Moreover, a preliminary rest cure not only determines the response to rest, but it allows time for an early lesion of the better lung to become partially arrested, so that when

the pneumothorax is eventually induced the less affected lung will be better able to withstand the added work. On the other hand, if one delays too long, adhesions almost invariably form which prevent complete compression Therefore, if when the patient is at rest the signs and symptoms increase, pneumothorax should be attempted at once before inseparable adhesions have formed in the involved side and an extensive lesion has developed in the less affected lung. Another reason against the indiscriminate use of pneumothorax is the danger in certain cases of complications. such as pleural effusion, for example.

A patient seldom develops an extensive lesion with cavitation in one lung without some involvement of the other lung which may vary from minimal to far-advanced disease, and for this reason the skill of the clinician and of the roentgenologist is taxed to determine whether or not in a given case a pneumothorax be advisable.

It is generally conceded that lesions involving more than one-third of the less affected lung contraindicate pneumothorax. This, however, is a relative and not an absolute rule, as a heavy infiltration in a small area may be more dangerous than a slight infiltration involving a larger area, so that an involvement cannot be estimated in mathematical terms alone, but must rather be judged by the relative activity of the lesion.

Cases of far-advanced slowly progressive disease sometimes demand palliative treatment for the control of fever, night-sweats, cough, and sputum, and in such cases if one can compress the area which contains large cavities and caseous infiltration the patients can frequently be made more comfortable.

Advanced cases are also subject to hemoptysis, which may be so abundant as to demand some form of radical treatment regardless of the condition in the opposite lung

Not infrequently far-advanced cases are encountered in which a pneumothorax cannot be made on account of adherent pleuræ. These adhesions are due to previous attacks of pleurisy with effusion during a moderately advanced stage of the tuberculosis, for the relief of which aspirations have been done without introducing air to maintain the separation of the pleuræ.

It is always a good policy to replace large tuberculous effusions with air, and in such cases it would seem advisable to maintain the pneumothorax until any indications for its discontinuance have been determined. The indications for and the contraindications to the induction of pneumothorax may be summarized as follows:

I. INDICATIONS

1 Acute caseous pneumonic conditions with severe cough and copious sputum in which cavitation is beginning, but which progress under ordinary rest measures, require induction early.

2. Fibrocaseous lesions with cavitation in one lung and minimal disease in the opposite lung usually require pneumothorax after improvement under ordinary rest measures has ceased.

3. Partially arrested cases with few symptoms, but in which the sputum is continuously positive, may require pneumothorax in order to obtain a negative sputum before being allowed to return home, especially if they are associated with young children.

4. Cases with pleural effusion, in which the effusion should be replaced by air.

5. Cases with recurrent hemoptysis.

6 Far-advanced hopeless cases in which pneumothorax makes it possible to control annoying symptoms.

II. CONTRAINDICATIONS

1. The invasion of one-third or more of the better lung.

2. Dense infiltration of a smaller area in the better lung

3. Tuberculosis elsewhere than in the lungs, as in the intestines or kidneys. Tuberculosis of the larynx is not a contraindication.

4. When the tuberculous invasion of the lungs is a terminal infection or is coincident with some general disease, such as diabetes, cirrhosis of the liver, or chronic nephritis.

In addition to these favorable and unfavorable indications, it should be noted that patients of a highly neurotic temperament usually do badly; and that patients with good resistance should first be treated by ordinary medical measures.

THE TECHNIC OF THE PROCEDURE OF INDUCTION

The reasons for the induction of a pneumothorax and the method should always be explained to the patient In our experience these patients are almost invariably anxious to have it tried. Care should be taken not to raise false hopes, as the pleuræ may be adherent and the induction impossible.

Before attempting the induction the chest should be thoroughly examined physically, by *x*-ray films, and fluoroscopically to determine the best site for the puncture In most cases this is in the axillary line between the fourth and eighth interspaces, though other sites may be tried if attempts in this area are unsuccessful

About forty-five minutes before the induction the patient is given a sedative, chloral hydrate and bromids being very satisfactory for this purpose, as they control nervousness efficiently without destroying the reflexes to the same extent as the opiates

The patient may lie on the good side on an ordinary office table, lying with a pillow under the midregion of the chest, so that the rib spaces are increased, the arm being drawn forward out of the way Other positions, such as the semi-erect, may be used, but it is advisable to use the same position each time, as intrathoracic pressures vary considerably with change of posture

The area is cleansed with ethereal green soap, iodin, and alcohol The skin can be frozen with ethyl chlorid, which also acts as an antiseptic, or anesthesia may be produced by the injection of 1 per cent. novocain with or without 1:15,000 adrenalin chlorid in advance of the needle until the pleura is reached. While the pleura should be thoroughly anesthetized, it is important to avoid puncturing the visceral pleura, thus producing a spontaneous pneumothorax. While adrenalin chlorid is of some benefit, in that it constricts the vessels so that the needle is less likely to become plugged with a blood-clot, yet the adrenalin frequently produces disturbing sensations in susceptible individuals. In one case this was so marked that the patient refused to allow the novocain solution to be used, and a quinin

and urea hydrochlorid mixture was substituted. If the adrenalin is omitted, however, there will be no action from the novocain.

After the area has been well anesthetized the skin and underlying fascia are incised by an iridectomy knife, care being taken in thin-chested individuals, in particular, to avoid puncturing the pleuræ. The incision is then ready for the insertion of the pneumothorax needle.

Several types of pneumothorax needles are available. The all-important factor in the selection of the needle is to choose one which will not easily puncture the visceral pleura. The needle should have a moderately large internal bore, a 16 to 14 gage being satisfactory, and the entrance of air through the needle should be controlled by a stop-cock. For cases in which adherent pleuræ are suspected it is well to use a needle with a hole in the side of the tip, so as to prevent its closure by pressure on the end. This model is also convenient because an obturator can be used which is more convenient than a stylet.

If the pleuræ are not adherent, the operator will perceive a diminution of pressure as the needle passes through the parietes, and when the manometer is connected it will register a negative pressure of from 30 to 80 mm. of water (as read from the manometer) and respiratory oscillations will be observed. As soon as the safe passage of the needle through the parietes is thus established it is safe to open the stop-cock and allow the negative pressure to aspirate some air—from 100 to 200 c.c. in the average case—through a sterile filter, after which air is introduced under slight pressure until about 300 c.c. have been introduced, or until the expiratory reading on the manometer is from about −10 to 0, when the inspiratory reading will vary from −40 to −20. Pressure readings should be taken after the introduction of each 100 c.c. of air. If the respiratory oscillations are very wide, the manometer tubing may be partially compressed and a mean pressure of from −15 to −10 mm. determined. The needle is then withdrawn and a pressure pad applied to prevent the production of a superficial emphysema.

If a free pleural space cannot be reached through the site of the first puncture, a second or third puncture may be tried, pro-

sema, which occurs after large needles have been used for the initial induction, or later, when high positive pressures are being maintained. Apart from slight discomfort for twenty-four to thirty-six hours no untoward symptoms result This possibility of emphysema can be lessened by the use of a pressure pad or cork after the operation and by the control of coughing.

Deep emphysema is a much rarer, but more serious, complication, which is most apt to occur at the initial attempt to institute pneumothorax in cases in which the pleuræ are adherent, so that air is introduced outside the parietal pleura and extends thence to the mediastinum Deep emphysema is accompanied by dyspnea and dysphagia, sometimes to an alarming degree, but these usually subside quickly

Pleural reflex not uncommonly occurs at some stage of the procedure, but most frequently happens when the pleura is acutely inflamed and, in consequence, is anesthetized with difficulty

In one of my patients each refill was accompanied by pain which extended over the entire side of the chest and into the neck, and on two occasions there was momentary fainting followed by weak heart action for two hours, but never any more serious symptoms

After the initial induction patients with pleural adhesions frequently suffer pain caused by the separation of adhesions This may be so severe as to require an opiate for relief

At the initial induction the needle may perforate healthy lung tissue and cause a spontaneous pneumothorax, or it may pierce a diseased portion of the lung, with resultant fresh infection of the pleura, or, in rare instances, it may perforate a cavity When this occurs the readings remain at atmospheric pressure or return to the same quite quickly after air has been introduced If there is still any doubt, a volatile substance may be put in the filter, which the patient will smell as it is exhaled if perforation of a cavity has occurred There is now being installed in our radiological department an equipment which will make it possible to do the pneumothorax inductions under

the fluoroscope, so that the operator will always know the exact position of the point of the needle.

Occasionally a ball-valve pneumothorax occurs when the pleural pressure becomes suddenly very high, with resultant displacement of the heart, mediastinum, and opposite lung to such a degree as seriously to embarrass the patient. In such cases it is necessary to insert one end of a tube into the pleura, the other end being carried under water so as to reduce the high pressure to that of the atmosphere.

The complications last cited are seldom encountered except where a compression is attempted as an emergency measure.

Cases in which gas embolism has resulted from the puncture of a pulmonary vein have been reported.

Pleural effusion occurs in about 40 per cent. of the cases in which pneumothorax has been instituted, occurring usually soon after the early inductions. The majority of effusions are serous and transient and never require any treatment; in other cases one or two aspirations suffice; while in a few cases the effusions become purulent, the fluid being either sterile or containing tubercle bacilli, and require repeated aspirations and irrigations.

The occurrence of some displacement of the mediastinum is frequently experienced and does not necessarily depend on the degree of pressure. Cases of complete pneumothorax with little or no previous pleurisy may not tolerate a positive pressure and, consequently, the mediastinum bulges most at the weak spot resulting from atrophy of the thymus gland. These cases complain of pain in the right second and third interspaces associated with a sense of ill-being and loss in weight. When the refill interval is extended and the pressure slightly reduced, these symptoms subside.

Cases of partial pneumothorax with adhesions or those which have had extensive pleurisy with resultant increased rigidity of the mediastinum will often tolerate high intrapleural pressure with little or no displacement of the mediastinum.

A flexible mediastinum is evidenced by a sluggish rise of pressure with relatively small oscillations, and by stationary manometric readings after the insertion of one or two consecu-

tive deciliters of gas For this reason it is important always to do the pneumothorax with the patients in the same position, and to have them try to breathe in the same way, as these factors affect the manometric readings

Occasionally when the needle is introduced for doing a refill the operator is surprised to find the respiratory oscillations reversed When the possibility that the needle is not in the pleural space has been ruled out, this reversal indicates a paradoxical action of the diaphragm, that is, the diaphragm moves up with inspiration and down with expiration. This condition may occur with high positive pressures or with low pressures just before the appearance of a pleural exudate, so that the patient should be put to bed and examined a few days later to see whether any fluid has appeared

Isolated case reports indicate that the pericardium, the heart, the diaphragm, and the large vessels have been perforated, but such instances are rare

Pleural adhesions are not necessarily a contraindication to pneumothorax, provided a pocket can be found which will hold a few hundred c c of air, so that a diseased portion of the lung can be compressed One cannot expect to institute a complete pneumothorax in more than 60 per cent. of the cases Even so, partial pneumothoraces frequently compress cavities and render the patients sputum-free In isolated cases it is possible to cut the adhesions and allow a more complete compression.

Physical and roentgenologic examination will not always determine whether a pneumothorax is possible, as sometimes the pleura may appear thickened on the x-ray film and yet a fairly clear pleural space may be found In all doubtful cases, therefore, an attempt to institute a pneumothorax should be made, for harm will seldom be done even if the attempt proves to be unsuccessful

CONCLUSIONS

Pneumothorax therapy is a tried and tested method in the treatment of pulmonary tuberculosis, and offers a means of recovery to some patients whose outlook is otherwise hopeless

The choice of cases and of the optimum time for the induc-

tion of a pneumothorax is a difficult problem, but in all cases which do not progress under an ordinary regimen of rest, pneumothorax should at least be considered, and if the condition of the other lung does not contraindicate it, the induction should be inaugurated at once.

Refills should be frequent and small rather than infrequent and large, and high positive pressures are to be avoided except in cases of partial pneumothoraces in which there is not so great a strain on the mediastinum.

When possible, fluoroscopic observations should be made to determine whether or not a negative pressure is sufficient to compress the lung completely, as, if so, positive pressures are not only not necessary, but are harmful

Pneumothorax therapy is a tedious process and requires patience, but to see patients in the prime of life returned to health and work is ample recompense for the effort.

T. E. JONES

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THE IMPORTANCE OF ESTABLISHING THE DIAGNOSIS IN SUSPECTED CASES OF VINCENT'S ANGINA

THE following 2 cases are reported with the object of pointing out that a diagnosis of Vincent's angina based alone upon positive smears and cultures of Vincent's organism in cases of ulcerated conditions of the throat may be very misleading, and if no further effort is made to establish the diagnosis serious consequences may result.

Case I.—A man, forty-six years of age, who was referred to the writer by Dr. John D. Osmond, was first seen on December 17, 1921. He was married and had 3 children living and well. He had never had any illnesses except tonsillitis and quinsy, having had attacks of the former, generally on the right side, ever since he was fourteen years of age; he had also had several attacks of quinsy on that side which were lanced. The Wassermann test was negative. In July, 1921, after having been treated for a sore throat for a couple of weeks, he had a hemorrhage from the throat. At that time Dr. Osmond took a section, which was reported to be non-malignant, but a smear showed the organism of Vincent's angina. Salvarsan was administered locally and systemically, but after from six to eight weeks of this treatment there was no improvement.

When I first saw the patient the physical examination was negative except for a large ulcer in the right tonsillar fossa which extended to the soft palate, the base of the uvula and the base of the tongue, and involved the anterior and posterior pillars. The border of the ulcer was thickened and was firm to

the touch; its base was not dirty, but was rather granular in appearance. One deep gland in the neck near the angle of the jaw was enlarged to approximately the size of a hazelnut.

A clinical diagnosis of carcinoma was made. A section taken for pathologic examination was reported to be chronic inflammatory tissue It was stained for tubercle bacilli and found negative A smear again showed streptococci and Vincent's organism, and the patient was referred back for further treatment He was later seen by two other consultants, each of

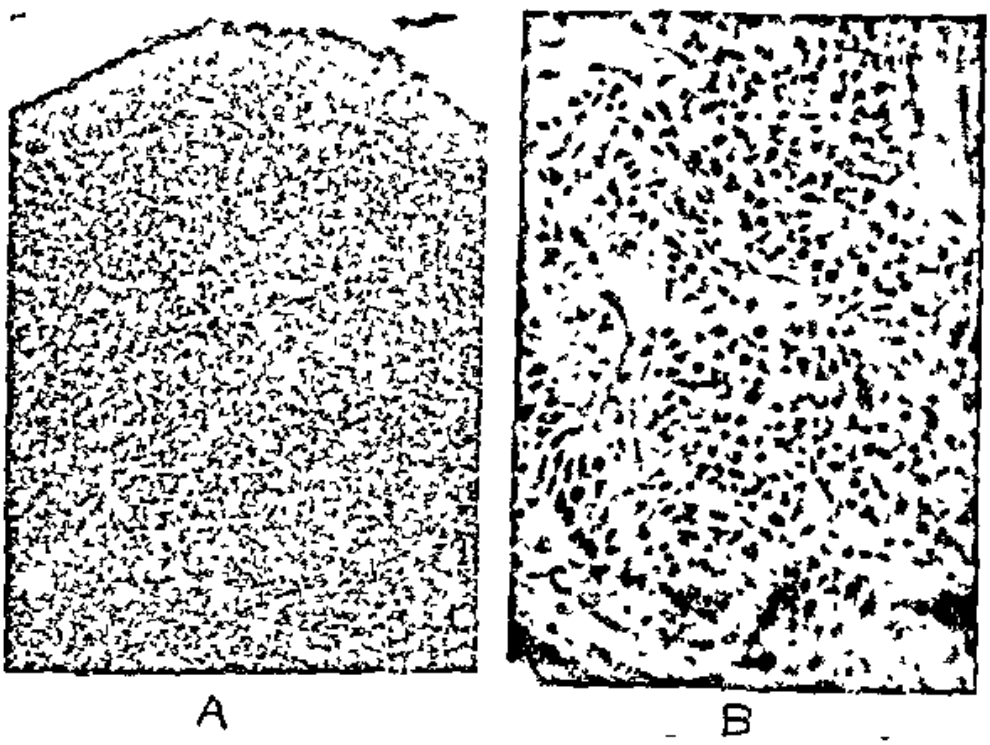

Fig 374 —Section from throat of Case I, reported by pathologist to be either carcinoma simplex or round-celled sarcoma A, × 130, B, × 350.

whom diagnosed the condition as lues For two months the patient received vigorous antiluetic treatment, without improvement A section was then taken and sent to Dr. Howard Karsner, who reported that the diagnosis lay between carcinoma simplex and round-cell sarcoma, the latter diagnosis being more probable because of the clinical history (Fig 374)

During the following three months the induration and extent of the ulceration increased, the size of the enlarged gland remaining unchanged

In March, 1922, in view of the last pathologic report, radium treatment was begun, the successive treatments being as follows:

March 17, 1922: 200 mg. radium (125 mg. in tubes screened with $\frac{1}{2}$ mm. of silver and six radium needles), distance $\frac{1}{8}$ inch, fixed in pack to conform with cavity; time, four hours—800 mg. hours.

April 10, 1922: 125 mg. radium screened with $\frac{1}{2}$ mm. silver, distance $\frac{1}{8}$ inch, time, two and two-thirds hours—335 mg. hours

Following the first treatment a reaction appeared in seven days, but was not very severe at any time. The gland-bearing area was treated with *x*-ray by Dr. Osmond.

On May 5, 1922 the ulcerated area was entirely healed, and on August 18, when the patient was again observed, he had gained 25 pounds and felt entirely well. He has remained well ever since.

Case II.—The patient, an unmarried man twenty-three years of age, was admitted to the Cleveland Clinic on June 16, 1923, with a history of having had trouble with his throat for almost a year. For this condition he had received three injections of salvarsan in November, 1922, and had used gargles constantly. The Wassermann test had repeatedly been negative, but salvarsan had been given on account of the presence of Vincent's organism in smears During the preceding month the throat had been getting more painful in spite of various forms of treatment.

Examination on admission showed a mass in the pharynx and nasopharynx behind the right posterior pillar. This mass was 2.5 x 4 cm. in size and was elevated 1 cm on a sessile base It was slightly movable and firm—not ulcerated; its surface was covered with a yellowish-gray pus.

A clinical diagnosis of malignancy was made, but on account of differences of opinion the pus was examined and found to contain Vincent's organism and mycelial growths. For some weeks the patient received local applications of salvarsan, potassium chlorate washes, and potassium iodid by mouth, with

no improvement. A section was taken and sent to Dr. Allen Graham, who made a diagnosis of sarcoma (Fig 375).

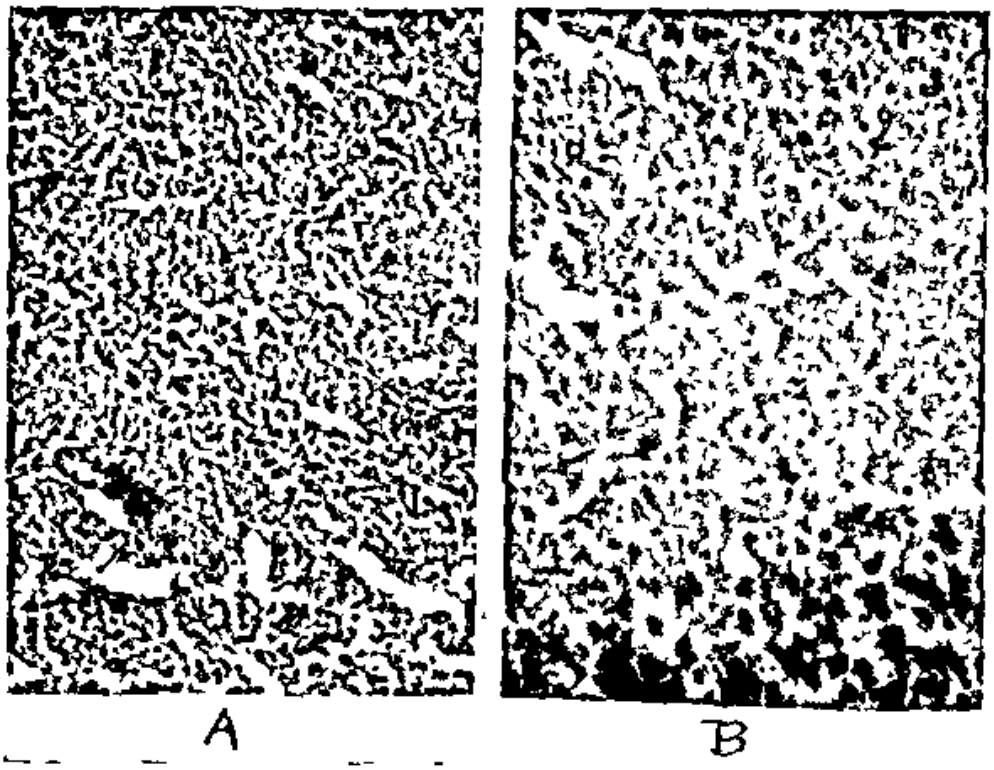

Fig 375 —Section from throat of Case II reported by pathologist to be sarcoma A, × 130, B, × 350

The following treatments were given·

Radium treatment July 12, 1923· Eight needles—total 62½ mg —inserted into growth at various points, time, nine hours. Total dose, 562½ mg hours

x-Ray treatment by Dr Portmann July 30, 1923

Place	K V	M A	Distance cm	Filter	Time minutes
Right neck	200	5	50	Copper, 75 mm	49
Left neck	200	5	50	Copper, 75 mm	49
Posterior neck,	200	5	50	Copper, .75 mm	34

The radium reaction appeared in seven days and entirely subsided in four weeks, when the tumor had disappeared

The patient was seen in May, 1924, when he was entirely well and showed no evidence of recurrence

DISCUSSION

It is generally agreed that Vincent's organisms are often found in apparently normal mouths. Their mere presence, therefore, may be considered as harmless. The number may be greatly increased, however, under bad hygienic conditions, when they may become pathogenic. Especially would this be true in the presence of an ulcerated condition due to a neoplasm. In such cases the ulceration and necrosis may tend to obscure the real pathologic process. The cases cited above offer striking evidence of the fact that the presence of Vincent's organism in an ulcerated condition of the throat does not establish the diagnosis of Vincent's angina, and that much time will be lost if we wait for a negative throat culture before making a further investigation to ascertain the exact nature of the lesion. It is urged that biopsy be done early, and that it be repeated as frequently as the progress of the individual case may indicate. The clinical picture is quite distinctive and is the most important factor in establishing the diagnosis

O. P. KIMBALL

DEPARTMENT OF INTERNAL MEDICINE

A FUNCTIONAL TEST FOR THE DIFFERENTIAL DIAGNOSIS OF HYPERTHYROIDISM

THE 2 cases cited below will serve to show the importance of establishing the differential diagnosis in mild cases of hyperthyroidism because many conditions characterized by an unstable sympathetic nervous system present symptoms which closely simulate those of hyperthyroidism.

Case I.—A young clergyman and college instructor twenty-three years of age complained of nervous exhaustion and fatigue which had persisted for three years. This had been so severe as to make necessary each year a stay of a month in a hospital under close observation and study by various internists, who each time made the diagnosis of nervous exhaustion

On March 6, 1923 this patient came to the Cleveland Clinic because of intense nervousness, palpitation, and fatigue. Physical examination revealed a normal robust young man weighing 161 pounds No exophthalmos was present and no ocular motor disturbance, there was a slight but definite tremor of the hands. The pulse was 134, the blood-pressure 130/80, the basal metabolism +25 The thyroid showed only slight enlargement, with no increase in blood-supply. There was a constant elevation of temperature which had ranged between 99° and 100° F. throughout the preceding month.

Because of the previous history and the diagnosis of neurocirculatory asthenia which had previously been made a functional thyroid test was made. He was given 50 grains of sodium bromid, and 10 mg. of iodin daily. On the fifth day he reported

that something was making him a great deal more nervous and that he could not sleep at all The basal metabolism was +33 at the end of the first week, when, on account of the nervousness and insomnia, the iodin was stopped, the bromid being continued. The metabolism at the end of the second week was +32, and in spite of the large doses of bromids and the enforced rest the metabolism persisted at approximately +30

A thyroidectomy was performed on May 2d, at which time the patient's weight had dropped from 161 to 156 pounds. The beneficial results of the operation were immediate and continuous. The patient has worked hard throughout the entire school year, carrying more work than ever before, his weight at the close of the year being 210 pounds; and he has experienced no abnormal fatigue, nervousness, or palpitation

Case II.—During the recent draft a young chemist thirty years of age had been judged unfit for service because of rapid heart action, and a diagnosis of exophthalmic goiter was made. Since that time he had had attacks of palpitation, unusual weakness, and periods of great mental disturbance He complained especially of pressure in the chest and of air-hunger.

The physical examination showed a very tense condition, with slight jerking and involuntary contractions of the muscles The pulse was 100 and the blood-pressure 110/70. The eyes were prominent, but there was no definite exophthalmos; there was slight but definite lagging of the upper lids The hands were cyanosed when pendant, and on extension showed a definite tremor. The thyroid was moderately enlarged, firm and smooth, with no increase in the blood-supply. The temperature was practically always above 99° F., the basal metabolism was +10.

The patient was given a functional thyroid test of 50 grains of bromid and 10 mg. of iodin daily. At the end of the first week the patient was considerably less nervous, with a metabolism of −9. He was sleeping well, but still complained of spells of palpitation and of the unusual air-hunger. At the end of the second week the metabolism was still −9, but the

patient seemed as unhappy and as neurotic as when the test was started.

On account of this negative result of the test for hyperthyroidism a period of rest and recreation was prescribed, and the patient was sent to the country, where he remained for two months, at the end of which time he had gained 6 pounds in weight and felt considerably better. After his return to work, however, the attacks of palpitation and air-hunger returned. For a period of seven months the patient was treated as a case of neurasthenia, with increased rest and sedatives. At the end of this time, since from his point of view very little change for the better had taken place, he insisted on a thyroidectomy, which was performed Histologic examination of the thyroid showed only a colloid goiter, and during the three months which have passed since the operation we have been unable to see any definite improvement. The patient still has attacks of palpitation, air-hunger, tremor, and cyanosis, in fact, all the symptoms of an unstable sympathetic nervous system.

These 2 cases are typical of more than 100 that have been carefully studied. In each case in which the thyroid gland was found to be extremely sensitive to iodin a definite diagnosis of hyperthyroidism was made, which was confirmed by improvement after thyroidectomy in all cases in which the operation has been performed. On the other hand, in the cases in which the thyroid metabolized the iodin and stored it without any increase in the rate of heat production, it was concluded that the thyroid was functioning normally and that no benefit would result from thyroidectomy. This conclusion also has been confirmed in those cases in which thyroidectomy has been performed by the lack of improvement after the operation (Fig. 376). In such cases the search for some other cause for the nervous symptoms must be persistently made.

Discussion.—The results of the studies of the physiology and physiologic chemistry of the thyroid gland which have been made during the last fifty years can be summarized as follows:

1. The thyroid gland controls the rate of heat production above the myxedema level. Most of our physiologists believe

that the all-important function of this gland is to maintain the metabolism at its normal rate

2 The normal function and histologic structure of the thyroid gland is dependent upon its iodin content. Every study that has been made emphasizes the intimate relation between iodin and thyroid function It has been the common observation and teaching that iodin intensifies thyroid activity in cases of definite hyperthyroidism This observation, together with the abundance of scientific data showing the intimate relation

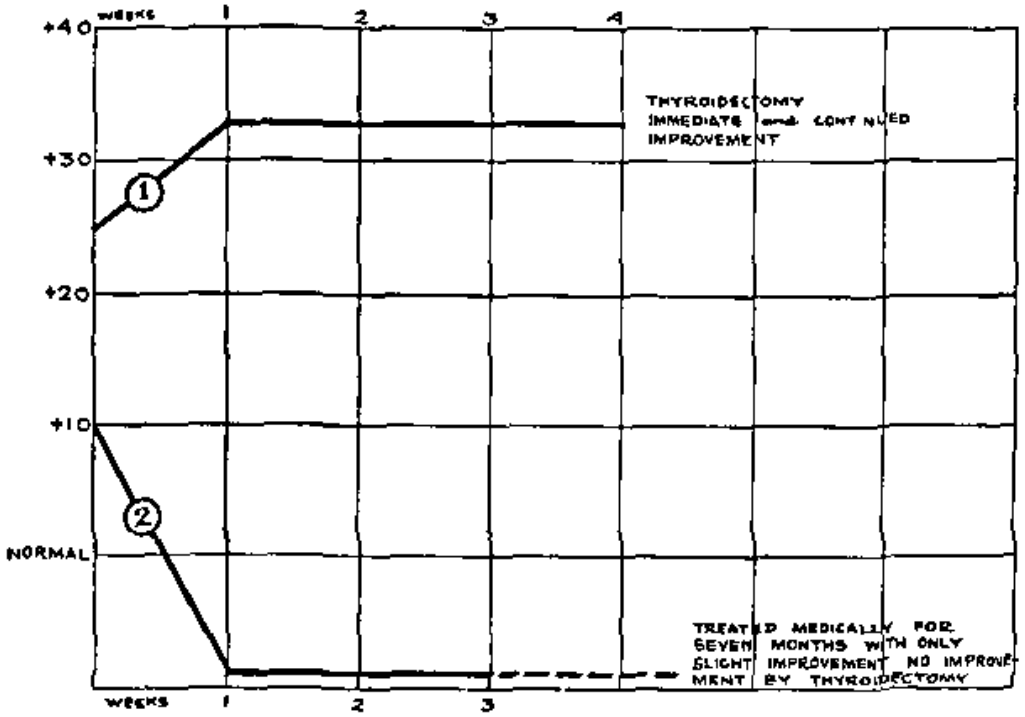

Fig 376—Chart illustrating the application of administration of iodin as a test of thyroid function in Cases I and II described in the text

of iodin to normal thyroid activity, is the basis of this study which has been illustrated by the case histories summarized above

CONCLUSION

As has been pointed out in the given cases, a comparatively small daily dose of iodin (10 mg daily is sufficient), together with a large daily dose of bromid (50 gr. of sodium bromid), is a valuable diagnostic measure in establishing the differential diagnosis of hyperthyroidism in doubtful cases It should be

emphasized that this medication is used for diagnosis only for a limited period, never as treatment, provided the diagnosis of hyperthyroidism is established. The patient must be watched closely, a careful observation being made at least once a week, with a recheck of the basal metabolism.

From our observation and postoperative studies of these cases we feel that this method of study is a valuable index to the function of the thyroid in any given case.

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STREPTOCOCCUS VIRIDANS ENDOCARDITIS

SUBACUTE bacterial endocarditis is a disease of very insidious onset, is protracted in its course, and has a very high mortality. For a number of years this disease has been of intense interest to internists, but because in some cases the spleen may be so enlarged as to simulate Banti's disease, while in others hematuria is a prominent symptom, these cases may be referred to a surgeon or genito-urinary specialist. Thus, in the following case the patient was referred to a genito-urinary specialist because of the presence of hematuria.

REPORT OF CASE

The patient, a young woman twenty-three years of age, was first seen on February 9, 1923, her chief complaints being fever, weakness, and hematuria. At the age of twelve she had had tonsillitis, followed by endocarditis, and shortly afterward her tonsils were removed. Since the above illness she had tired easily and had had considerable shortness of breath on exertion. One year later, at the age of thirteen, she had had a minor operation for an abscess of the cervical glands on the left side following an acute infection of the nasopharynx.

The history of the present illness dated back to the last week in November, 1922, when she returned from a football game feeling very tired. It was found that she had a slight elevation of temperature, and examination of the urine showed the presence of a number of pus-cells. She went to bed and was treated with urinary antiseptics, and in the course of three weeks felt much better. She began to feel much more exhausted during the last week in December, 1922, when it was found that her

temperature was varying from 99° to 101° F. During the month of January, 1923 this increased temperature continued, sometimes accompanied by slight chills, and the exhaustion increased During the ten days before she came to the Clinic she had complained of sharp pains in the calf of the right leg and in the lumbar region, and the urine had contained some blood. She also stated that she had had tender spots on her fingers and toes Because of the hematuria she was referred to my colleague, Dr W. E. Lower, for a genito-urinary examination As he realized that she had a general infection she was, in turn, referred to the writer for diagnosis

The patient was quite pale, with some flushing in the cheeks The eyes were normal, there was no tenderness over the sinuses; the teeth were in good condition, the tonsils were absent. Physical examination gave no evidence of disease of the lungs, and this negative finding was confirmed by the roentgenogram. The heart was enlarged slightly to the left, and over the entire precordium a blowing systolic murmur was heard, which was transmitted to the left axilla and back. Her pulse was regular and rhythmic, of full volume—rate 96, the artery walls were not thickened. The systolic blood-pressure was 134, the diastolic, 60; the temperature was 101 8° F

The examination of the abdomen showed the spleen to be readily palpable and tender The right kidney, which seemed to be enlarged, could be easily palpated, and the lower pole was very tender The left kidney could not be felt There were two small hemorrhagic areas in the right lumbar region There were no petechiæ on the lower extremities

The urine showed a faint trace of albumin and an occasional red cell and leukocyte The blood-count showed 4,380,000 erythrocytes, 7200 leukocytes, and 80 per cent hemoglobin The differential blood-count showed polymorphonuclear leukocytes, 85 6 per cent , polymorphonuclear basophils, 0 5 per cent , small lymphocytes, 9.5 per cent , large lymphocytes, 9 5 per cent.; and transitionals, 3 per cent. No nucleated red cells were seen in the examination of the stained smear. The Wassermann reaction was negative A blood-culture showed numerous

colonies of Streptococcus viridans, 22 colonies being counted in one plate.

The type of temperature shown during the stay in the hospital is illustrated by the accompanying chart (Fig. 377).

After the patient left the hospital she gradually grew worse. She was given small intravenous doses of cacodylate of soda and neosalvarsan, but these drugs seemed to have no effect on the progress of the disease. A short time before her death on May 13, 1923, she had a slight lesion of the pons. In the later stages of the disease the pallor became more marked and there

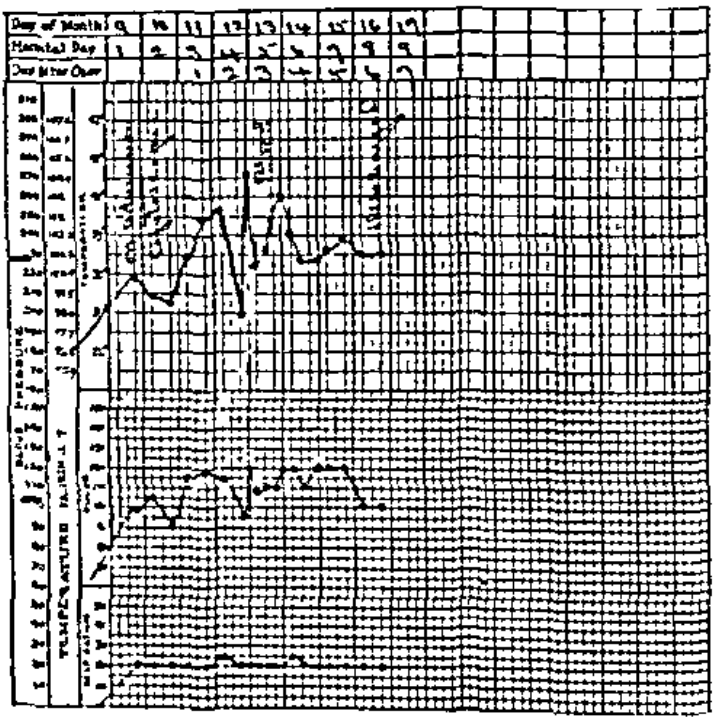

Fig. 377.—Temperature chart of patient with Streptococcus viridans endocarditis.

was some slight puffiness of the eyes and of the feet. Three other blood-cultures were made, all of which showed colonies of Streptococcus viridans. In the last blood-culture as many as 258 colonies were counted in one plate. The patient became comatose four days before her death.

GENERAL DISCUSSION

Three distinct types of endocarditis may be mentioned: (1) rheumatic, (2) syphilitic, and (3) bacterial. Bacterial endocar-

ditis may be acute or subacute, the former including those cases which run their course in less than six weeks

Among the organisms which may cause *acute* bacterial endocarditis are the Streptococcus hæmolyticus, the staphylococcus, the pneumococcus, the gonococcus, the influenza bacillus, and the meningococcus. As Libman[1] has stated, in these cases the heart lesions are vegetative and ulcerative, and the metastatic lesions are of a suppurative type

About 95 per cent. of the *subacute* cases are due to the anhemolytic streptococcus (Streptococcus viridans), the remaining 5 per cent being caused by the influenza bacillus. Subacute bacterial endocarditis is not a rare disease Within the past year the writer in a general consulting practice has seen 16 cases. In 1921 Libman stated that up to that time he had seen over 300 cases of this condition

ETIOLOGY

The etiologic significance of the age incidence of subacute bacterial endocarditis is indicated by the fact that while the majority of cases seem to be between the ages of ten and fifty, the highest incidence is between the ages of twenty and thirty, which is the period during which the incidence of valvular heart disease is the highest

It is often difficult to decide the portal of entry by which the bacteria make their way to the blood-stream Among 58 cases in which Blumer[2] mentions the portal of entry, the teeth were responsible in 17, the tonsils in 16, the female generative organs in 13, the bronchi in 5, wounds and injuries in 4, the gall-bladder, the male genitalia, and furunculosis each in 1

It is interesting to note that subacute bacterial endocarditis nearly always affects a valve which has been previously damaged by rheumatic endocarditis, and few cases are recorded in which the disease has been associated with congenital heart disease. It seems probable that in these cases the direct cause of the disease is the lowered resistance of the heart to streptococcal invasion

PATHOLOGY

A consideration of the pathology of subacute bacterial endocarditis shows that the disease is a general septicemia, with localized involvement of the heart and embolic manifestations in various organs.

The cardiac lesions, as stated above, are engrafted on a previously damaged valve, but, in addition, there is frequently an involvement of the mural endocardium and of the chordæ tendineæ. There is very slight impairment of the myocardium, and the pericardium is affected in only a small proportion of cases The lesions of the valves are proliferative rather than destructive, taking the form of small verrucose excrescences or larger polypoid outgrowths. The valves on the left side of the heart are usually involved, the mitral much more frequently than the aortic. Pronounced lesions of the coronary arteries are rare

Horder[4] reports that in a series of 118 autopsies in cases of bacterial endocarditis the distribution of the valve lesions were as follows:

Mitral cusps only	38
Aortic cusps only	22
Mitral and aortic cusps	63
Tricuspid with mitral or aortic valves, or with both	14
Pulmonary cusps with mitral or aortic valves, or with both	7
Mural infection (auricular)	43
Mural infection (ventricular)	8

The general toxemia may be evidenced by swelling of the lymph-nodes of the mediastinum and peritoneum; by cloudy swelling of the myocardium, liver, and kidneys; and by degenerative changes in the pancreas and adrenals.

The vascular lesions constitute one of the most interesting features of the disease. Embolic aneurysm and embolism of various arteries, with resulting infarction of the viscera, may occur Among 21 cases of arterial obstruction collected by Blumer[2] the pulmonary artery was affected in 4, the middle cerebral artery in 3; the aortic and brachial arteries each twice; the radial, coronary, iliac, and nasal arteries each in 1; the anterior

tibial, basilar, and mesenteric arteries each once, and the internal carotid, splenic, and hepatic arteries each in 1. Horder found infarction of the spleen in 47 of his 150 cases, and infarction of the kidneys in 46. A striking feature of the embolic lesions of subacute bacterial endocarditis, as contrasted with those of acute bacterial endocarditis, is the absence of suppuration in the former.

Thrombophlebitis occurs in about 6 per cent of the cases

The kidney lesions which are of particular importance have been carefully described by Lohlein and by Baehr.[1] The latter states that "the salient features of the lesion which serve to differentiate it from other types of glomerular disease are, first, the involvement of one or more loops of a variable number of glomeruli, second, the absence of any visible disease in the uninvolved glomeruli and in the uninvolved portions of affected glomeruli, and third, the association in most of the bacterial cases of all stages of the glomerular process, often seen in a single microscopic section" On account of the patchy distribution of the lesions the kidney function is most seriously impaired.

CLINICAL SYMPTOMS

The onset of the disease may be very insidious In the majority of cases there is a period of from two to four weeks of ill health, during which the patient runs a slight temperature The onset of the fever may be accompanied by sore throat, headache, and slight chilliness, with general aching and soreness There may be arthritic pains, but any definite swelling of the joints is rare The presence of fever, slight cough, sweating, and loss in weight may suggest tuberculosis Frequently the presence of chills with fever may suggest malaria

The presence of persistent fever is one of the dominant features of the disease, and for a long time it may be the only symptom Thus, for week after week and month after month, a persistent elevation of temperature of from $1\frac{1}{2}$ to 2 degrees may be the only indication of disease, the presence of previously existing murmurs obscuring the fact that a fresh endocarditis has developed. The temperature may be of the continuous

type, resembling that of typhoid fever, or in other cases with marked chills it may be of the remittent type, varying from normal to 105° F., thus suggesting malaria, as in the case of a doctor who was treated for malaria for several weeks (Fig. 378). In such cases, however, the elevations of temperature do not occur with the quotidian or tertian regularity which is characteristic of malaria. Toward the end of the disease afebrile periods lasting for several days may give a deceptive promise of recovery.

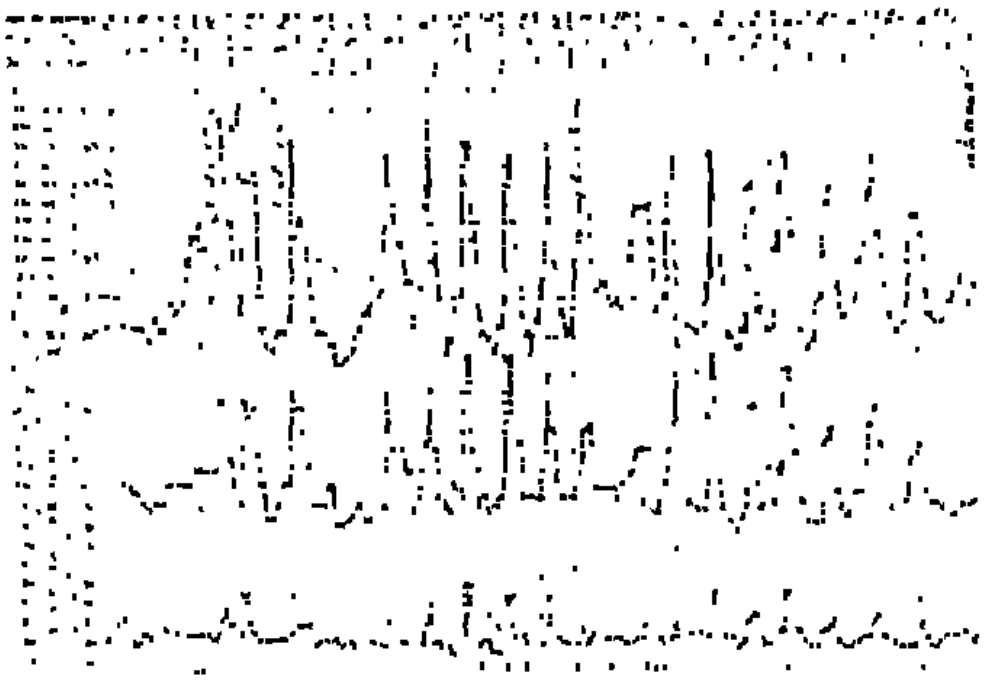

Fig 378.—Chart showing malarial type of temperature in a case of Streptococcus viridans endocarditis

In many of my patients headache has been a very troublesome symptom early in the disease, but more particularly in the later stages. Some patients complain of cardiac pain, palpitation, and shortness of breath, but these usually occur in the later stages of the disease when the embolic manifestations are the most important features. There may be pain in the region of the kidneys due to renal infarction, and infarction of the spleen may be present, with enlargement and tenderness of that organ. The patient may complain of tender spots on the fingers and toes. Disturbances of vision, monoplegia, hemiplegia, and aphasia may result from embolism of the cerebral

vessels In some patients delirium may be so marked as to suggest meningitis

PHYSICAL FINDINGS

The findings of the physical examination depend upon the stage of the disease. Early in its course the elevation of temperature may be the only abnormal sign, but later there is a well-marked pallor of the skin, with slight puffiness of the face Late in the disease, in the majority of cases, the skin shows a diffuse yellowish-brown color, often patchy in character, which is especially marked about the face Libman has emphasized this pigmentation of the skin and has characterized it as a "cafe au lait" tint. Petechiæ occur in the skin or mucous membranes, most commonly on the extremities, the lumbar region, the axillæ, the neck, the palpebral conjunctivæ, and the mucous membranes of the mouth They are apt to appear in crops which are synchronous with the development of embolic lesions elsewhere Occasionally, as in a recent case that came under my observation, the hemorrhagic areas on the neck may be at least $\frac{2}{3}$ cm in diameter. Other skin eruptions of the nature of an erythema multiforme and urticaria have been described Subungual linear hemorrhages, which look like splinters under the nail, have been mentioned by Blumer, Horder, and others. Clubbing of the fingers is often seen in the protracted cases.

The occurrence of the so-called "Mullin's or Osler's nodes" in the pads of the fingers and toes and in the thenar and hypothenar eminences is one of the most characteristic features of subacute bacterial endocarditis, and is of pathognomonic significance. Mullin, of Hamilton, Ontario, first called Osler's attention to these nodes, which he describes as follows "The spots came out at intervals as small, swollen areas, some the size of a pea, others a centimeter and a half in diameter, raised, red, with a whitish spot in the center I have known them to pass away in a few hours, but more commonly they last for a day or even longer. The commonest situation is near the tip of the finger, which may be slightly swollen." These nodes are painful and seem to be in the skin, resembling the wheal of urticaria They are not hemorrhagic

Examination of the heart often elicits tenderness on pressure over the sternum. There is increased activity of the heart, which is slightly enlarged, the enlargement increasing in the late stages of the disease. A mitral systolic murmur is most frequently noted, but later a systolic or diastolic bruit may be heard in the aortic or pulmonary area. Occasionally a loud rasping tricuspid murmur may develop. Signs of cardiac decompensation are very rare, but they sometimes occur late in the disease.

The spleen is palpable, often tender, and may be so enlarged as to simulate Banti's disease. At times a friction-rub can be heard over this organ.

As a result of embolism of the arteries many interesting physical signs may develop. Embolism of the central artery of the retina may cause blindness. Retinal hemorrhages are noted in about 10 per cent. of the cases. Pulmonary or coronary embolism may cause sudden death. Embolism of the mesenteric arteries may cause symptoms of some acute abdominal disease. If the vessels of the extremities are involved, gangrene may result Lesions of the cerebral vessels may cause aphasia, monoplegia, or hemiplegia.

The urine usually shows a trace of albumin and some casts Red blood-cells are found in at least 50 per cent. of the cases. Sometimes there is definite hematuria and the patient may have attacks of renal colic from the passage of blood-clots.

There is always a steadily increasing anemia of the secondary type throughout the disease. Early in the disease the red blood-cells range between 3,500,000 and 4,000,000 per cubic millimeter, but as the disease progresses the count often drops to between 2,000,000 and 3,000,000. At the same time the hemoglobin drops from between 75 and 85 per cent. to from 45 to 50 per cent. In the majority of cases the leukocyte count varies from 10,000 to 14,000, but occasionally a leukocytosis of from 20,000 to 30,000 is seen. On the other hand, it is not unusual to find a leukocyte count of from 4000 to 8000. As a rule, there is a slight relative increase in the polymorphonuclear cells.

Blood-cultures are always positive at some stage of the dis-

ease if a proper technic is used. A positive blood-culture has been obtained in every one of the last 10 cases in which I have had the opportunity to have cultures made. We have used a strong beef-broth, using three times the proportion of meat ordinarily used in the preparation of culture-media, have added peptone and salt, and have adjusted the reaction to the neutral point, adding glucose later. Before plating we add to one of four tubes, each containing 10 c c of the medium, ½ c c of blood, to the second tube, 1 c c. of blood, to the third, 1½ c c., and to the fourth, 2½ c c., the smaller amounts being used because the deeper the color, the greater the difficulty in distinguishing fine colonies. The plates are wrapped in a large piece of filter-paper and are placed in a small stand in a jar in the bottom of which below the level of the plates there is a small amount of water. The jar should be well covered and placed in an incubator at 37.5° C. Colonies usually appear within twenty-four hours, but at least three days should be allowed to elapse before the culture is pronounced negative.

The course of subacute bacterial endocarditis is prolonged, lasting from three to eighteen months. Sometimes there are remissions in the disease that are very deceptive, but with few exceptions the course is progressively downward, and is accompanied by increasing weakness and loss in weight. The prognosis is bad, recovery occurring only in from 1 to 2 per cent. of the cases. Death may result from exhaustion and toxemia, from embolism—cerebral or pulmonary—or from some terminal infection, such as pneumonia. In rare instances cardiac decompensation is the cause of death. The physician should always keep in mind the possibility of sudden death, and the friends of the patient should be warned that this may occur. I was impressed with this possibility by a case which was thought to be one of persistent malaria. I saw the patient in consultation the day after an intravenous administration of salvarsan, which had been followed by a sharp reaction which had persisted for twenty-four hours. I found the case to be one of subacute bacterial endocarditis, with the malarial type of temperature, and warned the family of the possibility of sudden death. On

the following day the patient died suddenly from pulmonary embolism. I feel sure that if the family had not received this warning, with an explanation of the true nature of the disease, they would have blamed the sudden death on the intravenous treatment with salvarsan.

A group of 23 mild cases in which the symptoms resembled those of neurasthenia, exhaustion, and anemia and in which blood-cultures positive to Streptococcus viridans were secured, have been described by Oille, Graham, and Detweiler.[6] These patients recovered.

DIAGNOSIS

Osler[7] has pointed out that the cardinal diagnostic features of subacute bacterial endocarditis are fever, the evidence of old valve lesions, embolic phenomena, and positive blood-cultures. To these I would add the following signs: enlarged spleen, petechial hemorrhages, hematuria, and tender spots on the fingers and toes, although the objection might be made that these conditions are simply evidences of embolism.

The diseases with which subacute bacterial endocarditis is most frequently confused are: (1) Rheumatic endocarditis, (2) influenza, (3) typhoid fever, (4) malaria, (5) tuberculosis, (6) pyemia or a concealed focus of suppuration, (7) pernicious anemia, (8) renal tuberculosis, (9) splenic anemia, (10) acute leukemia. If a careful history of the case is taken, keeping in mind the significance of an old valvular lesion and the cardinal symptoms of the disease, and if the observer looks in particular for an enlarged and tender spleen and petechial spots, and takes a blood-count and a blood-culture, there will be little difficulty in making the correct diagnosis, so that it is not necessary to take up in detail the differential points.

In a case of acute leukemia in which the writer found it difficult to establish the differential diagnosis the child had a temperature varying from 102° to 104° F., a blowing systolic murmur over the heart, a readily palpable spleen, and but slight enlargement of the lymph-glands, but the blood changes characteristic of leukemia did not manifest themselves until after the child had been under observation for two weeks.

The greatest diagnostic difficulty is found in establishing the differentiation between rheumatic endocarditis and endocarditis from Streptococcus viridans. Rheumatic endocarditis is usually accompanied by polyarticular arthritis, the frequency of joint involvement being in marked contrast to that seen in subacute bacterial endocarditis In the latter disease chorea, pericarditis, and erythema nodosum are rare, while in rheumatic endocarditis they are common complications. Negative blood-cultures would favor a diagnosis of rheumatic endocarditis

TREATMENT

The treatment of subacute bacterial endocarditis should be directed to prevention and to cure. Prophylaxis demands the elimination of foci of infection, this being particularly important in cases of valvular heart disease, in which the resistance of the patient and of the valves themselves is lowered to streptococcus infection The teeth should be examined regularly, the examination being supplemented by a roengtenogram to exclude apical infection In many cases devitalized teeth are a menace. Other foci of infection, such as sinusitis, infected tonsils, or chronic inflammatory conditions elsewhere in the body, should be eradicated.

With the onset of fever it is important that the patient be kept in bed and given an easily digested but nutritious diet and plenty of fresh air. Various drugs have been used to promote the comfort of the patient during the period of chills and fever. Quinin and salicylates give the patient the greatest comfort. Iron and arsenic should be given to combat the anemia

Up to the present time the one drug that offers the greatest hope of cure is cacodylate of soda given intravenously, 10 to 15 grains being given every two or three days for two weeks, the treatment being repeated after an intermission of one week. Capps,[3] in particular, has stressed the value of this treatment. The intravenous administration of mercurochrome has been tried, but so far without benefit. Vaccines and transfusions of blood, in some instances from a vaccinated donor, have been

tried repeatedly, but from the reports in the literature and from my own personal experience these have been of no value.

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DEPARTMENT OF INTERNAL MEDICINE

A CLINICAL DISCUSSION OF THE DIAGNOSIS, TREATMENT, AND PREVENTION OF DIABETES

DIAGNOSIS

As a rule it is not difficult to establish the diagnosis of diabetes. The presence of sugar in the urine leads to a fasting blood-sugar examination, and if this is high, a diagnosis of diabetes is made at once. There is a group of cases, however, in which the diagnosis is not so obvious, cases which require further diagnostic measures because of the presence of one or more various factors in the light of which the laboratory findings must be interpreted. Thus the presence of glycosuria must be interpreted in terms of the level of kidney permeability.

The presence or absence of sugar in the urine is determined by the point at which the renal filter becomes permeable to sugar. This permeability of the renal filter varies with the individual, and may be present at any concentration of sugar in the blood above 45 mg. per 100 c.c. Thus in an individual whose renal permeability lies between 300 and 350 mg. per 100 c.c., no sugar will be found in the urine when his blood-sugar drops to below 300 mg. per 100 c.c. In such a case, however, a high hyperglycemia is present, and if it is allowed to continue, as would be the case were the patient classified as a non-diabetic on the basis of no sugar in the urine, the destruction of the islands of Langerhans would continue, and, in consequence, the patient's carbohydrate tolerance would be continually decreased. Likewise, at a very low point of renal permeability sugar will be found in the urine at a very low blood-sugar level. On the basis of the glycosuria alone such a case may be classified as a dia-

betic even though no hyperglycemia exists, and the patient, in consequence, would needlessly be subjected to the vigorously limited diet of the diabetic, as well as to the mental suffering oc-

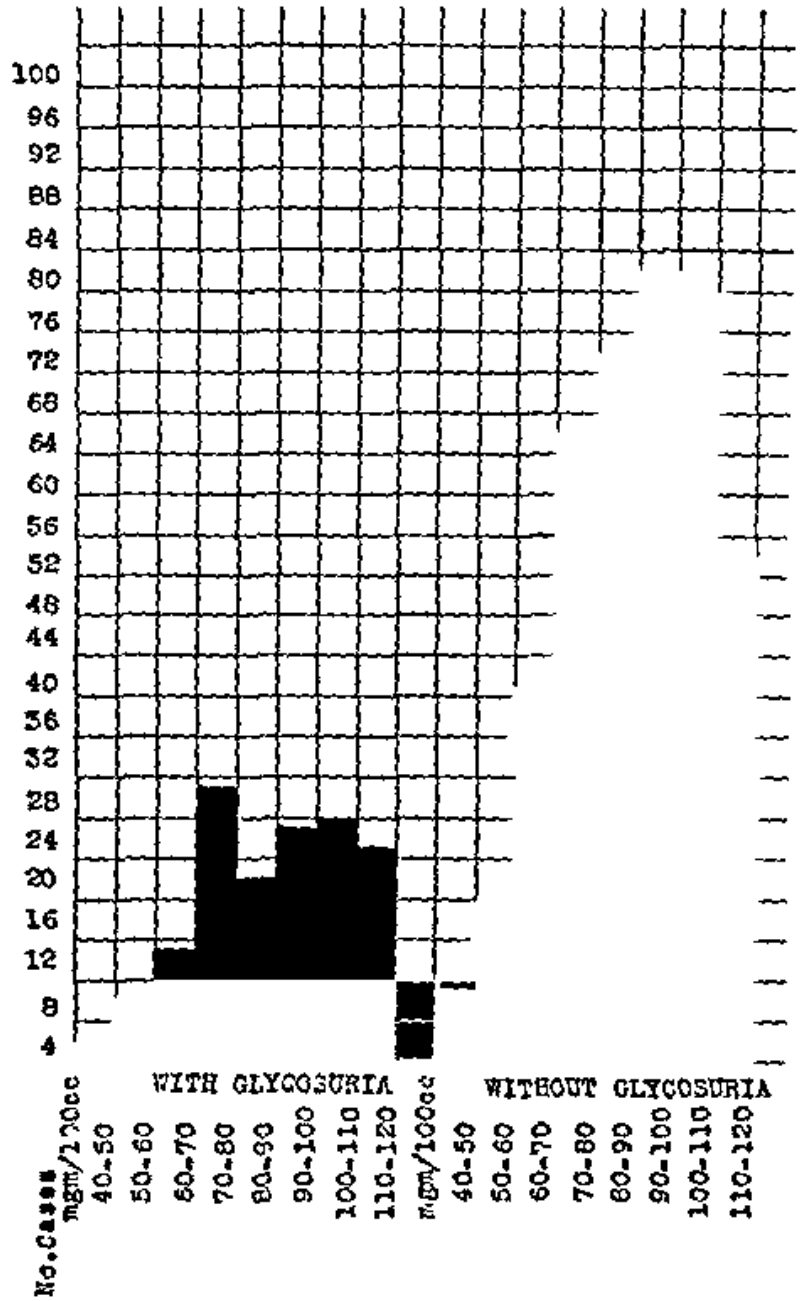

Fig. 379.—Relative number of cases with and without glycosuria at different blood-sugar levels (All below 120 mg. per 100 c.c.)

casioned by the conviction that he is the victim of an incurable disease

Figures 379, 380 show the point of renal permeability in a large series of cases. It is very evident that kidneys which are

permeable to blood-sugar concentrations below 120 mg. per 100 c.c. are not rare, and that we must take them into consideration in our every-day practice. Thus in my series of 714 ex-

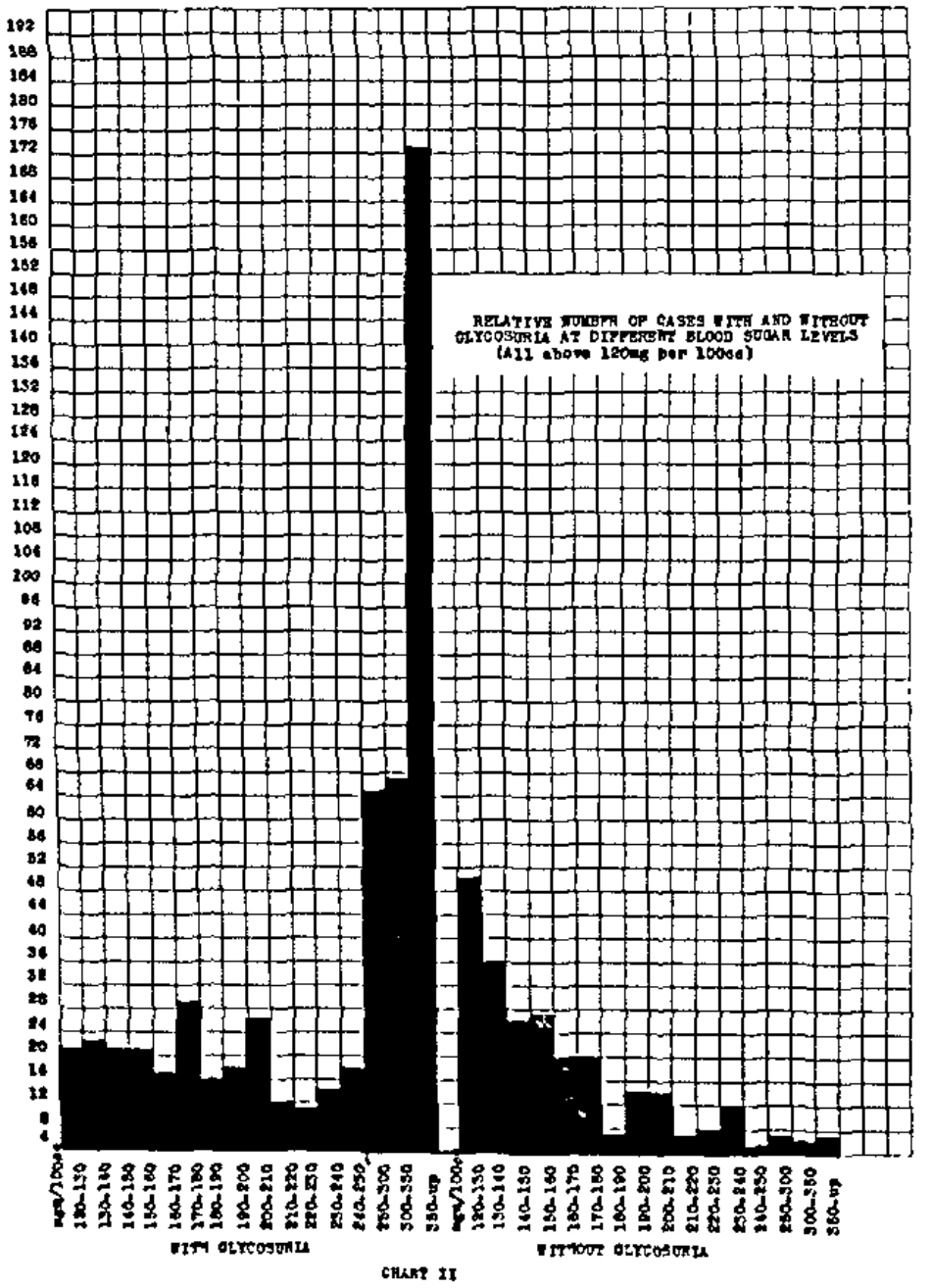

Fig. 380

aminations I found glycosuria associated with a normal blood-sugar concentration in 13.8 per cent., and hyperglycemia with no sugar in the urine in 18.3 per cent.

It is obvious, therefore, that we must rely upon blood-sugar

estimations rather than the presence of glycosuria as an index of the patient's condition. Blood-sugar estimations enable us not only to determine whether the blood-sugar concentration is above the level of the renal threshold, thus allowing sugar to appear in the urine, but also to know the actual concentration of the sugar in the blood, regardless of the presence or absence of glycosuria

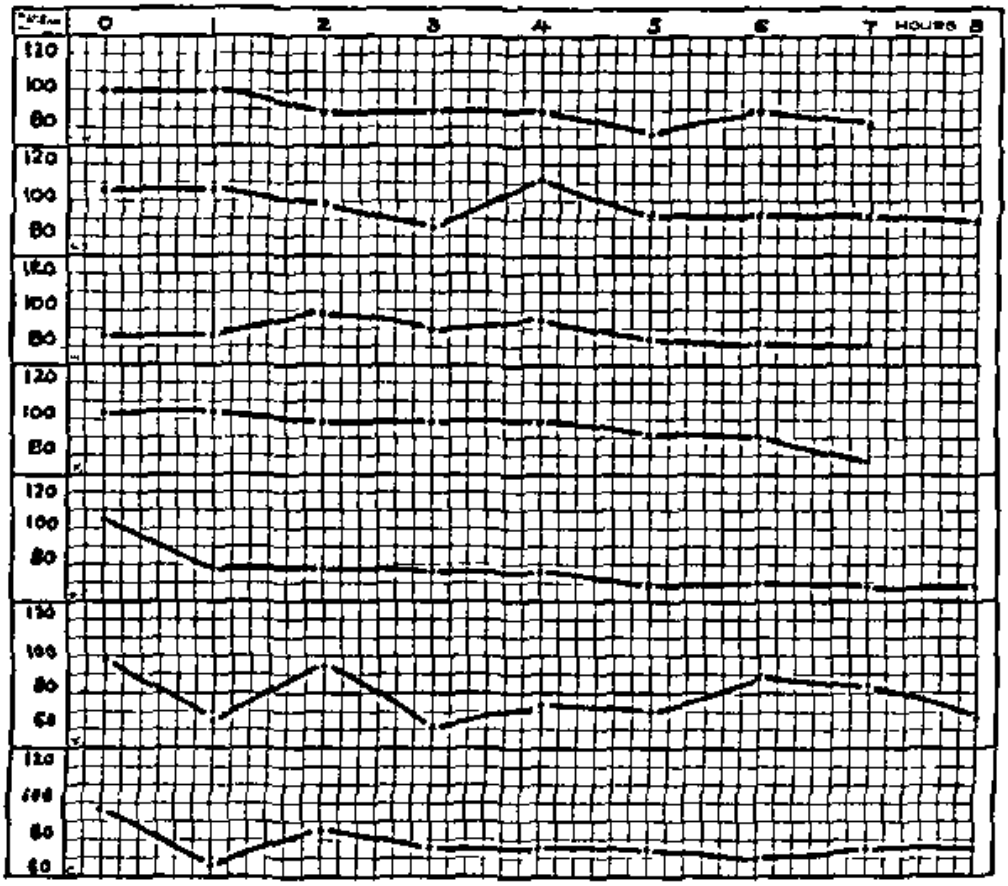

Fig 381 —Curves obtained from successive fasting blood-sugar estimations in 7 normal individuals

The interpretation of hyperglycemia, however, demands, further, a knowledge of the normal daily variations in the blood-sugar concentration. Therefore to determine whether or not the blood-sugar level of a normal individual varies during the day the following experiment was made. Hourly measurements of the blood-sugar contents in 7 normal individuals were made. All 7 individuals fasted all day, 2 of them not even drinking water *It is quite evident from the curves obtained in these*

cases (Fig. 381) that in a normal individual the blood-sugar level remains quite constant and shows practically no variations throughout the day. A fasting blood-sugar estimation, therefore, can be considered as a constant figure on which to base our determinations. This fact is of great importance.

After a meal, no matter how limited, the blood-sugar level in practically all individuals rises, returning to normal after a certain period of time. Therefore, blood-sugar estimations, unless made at the end of a sufficient period of fasting, are of little or no value in comparative studies.

G. S. Eadie,[1] in his experimental work on rabbits, investigated the stability of the blood-sugar content when no food was given with the following findings:

	A M			P M				
	10	11	12	1	2	3	4	5
Number of observations	34	25	15	15	16	19	17	12
The average blood-sugar content, mg. per 100 c c	118	118	120	115	112	112	114	117

Since the fasting blood-sugar determination can be considered a constant factor in a normal individual, we may conclude that a high fasting blood-sugar definitely establishes a diagnosis of diabetes. A low fasting blood-sugar does not necessarily rule out diabetes, however. The problem, therefore, is to differentiate between the diabetic and the non-diabetic in cases in which the fasting blood-sugar level is normal or only slightly above normal.

In such cases the one method of differentiation is the glucose tolerance test. If the individual's ability to utilize carbohydrates is definitely impaired, the fact will be shown by the glucose tolerance curve; if it is not impaired, blood-sugar estimations made at successive intervals of one-half, one, two, three, and four hours, following the ingestion of 100 gm. of glucose after a fasting period of at least twelve hours, will result in a normal curve (Fig. 382).

To establish the diagnosis of diabetes, therefore, unless the fasting blood-sugar content is above 180 mg. per 100 c.c., a

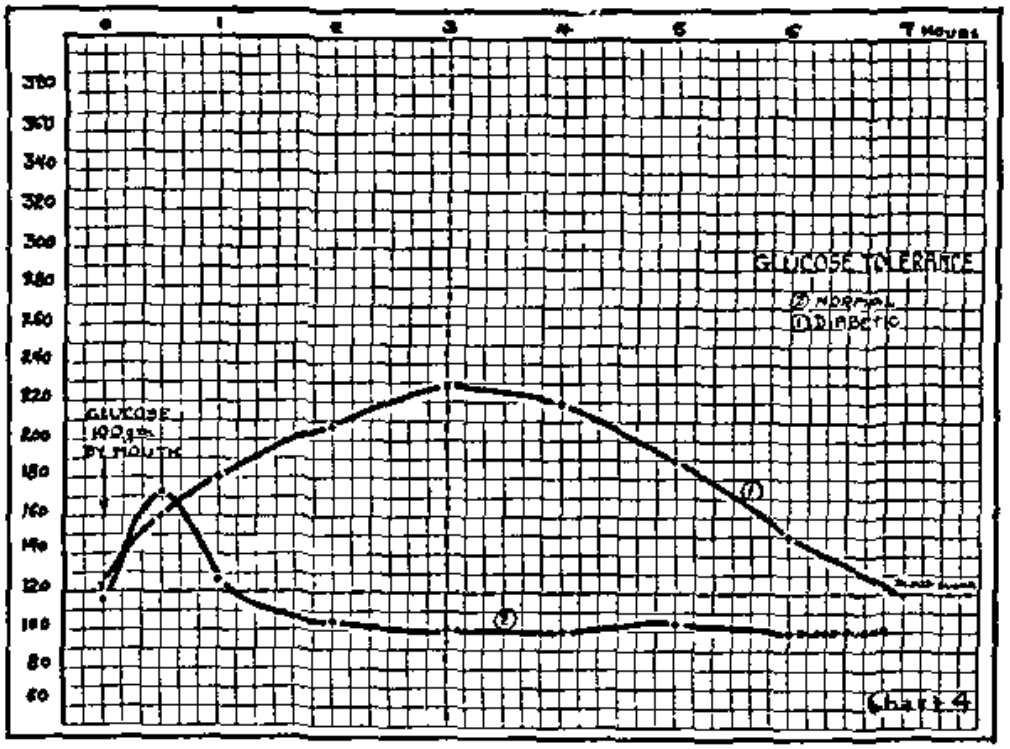

Fig 382.—Comparison of glucose tolerance curves in a normal (2) and in a diabetic (1) individual

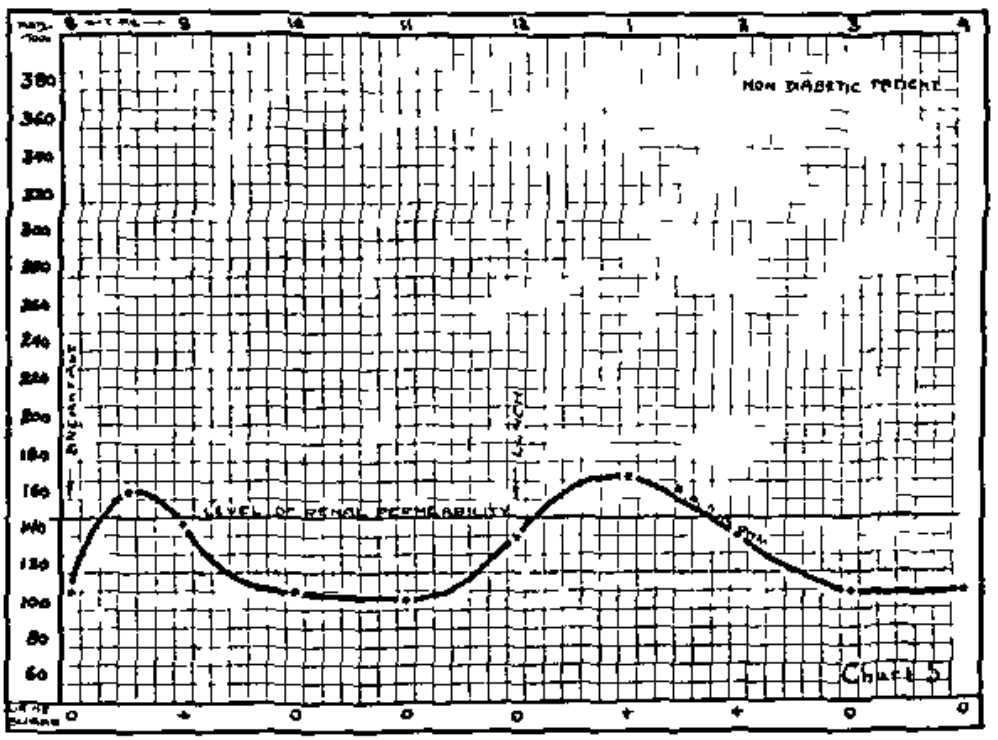

Fig 383.—Glucose tolerance curve in a non-diabetic, fasting blood-sugar, 110 mg per 100 c c

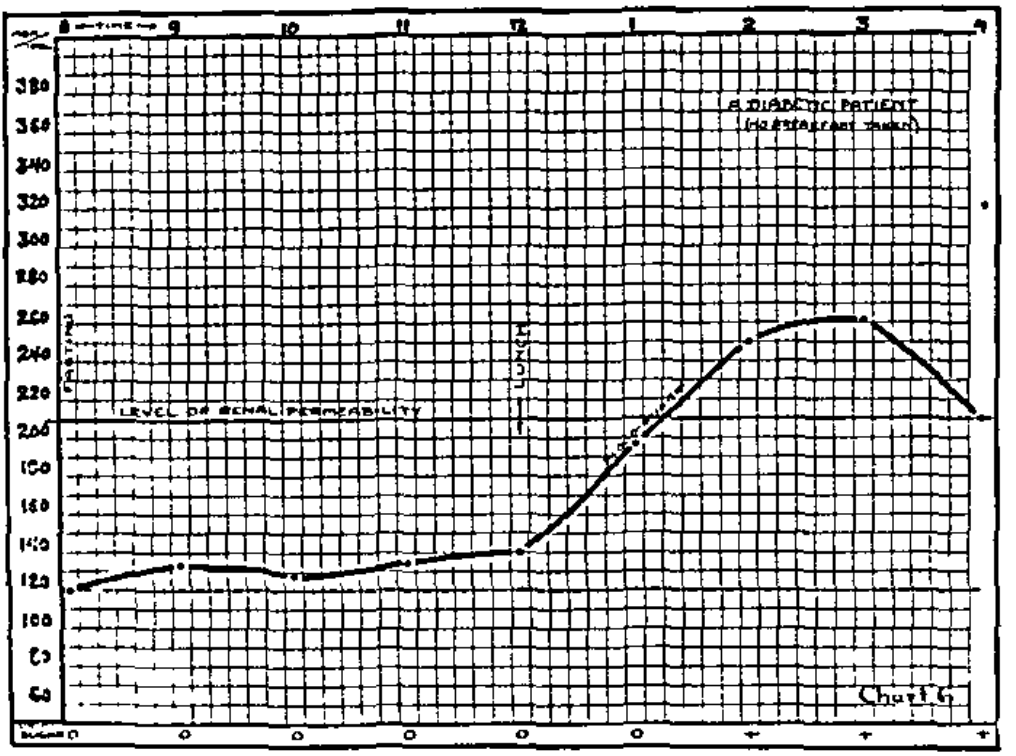

Fig. 384.—Glucose tolerance curve in a diabetic patient, fasting blood-sugar, 120 mg. per 100 c.c.

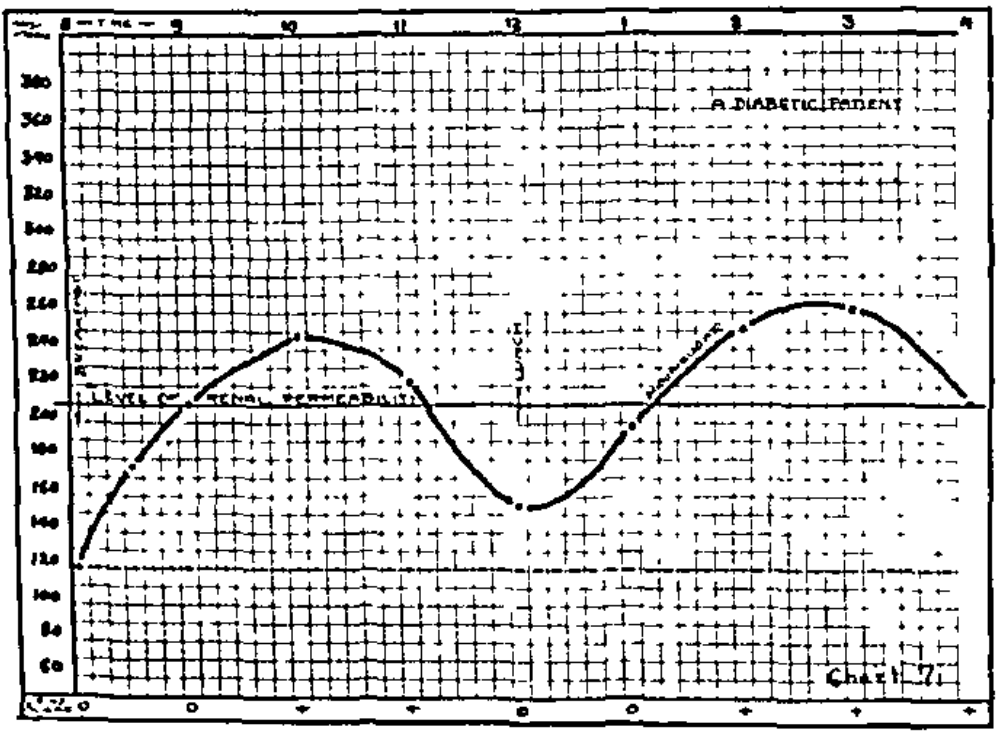

Fig. 385.—Glucose tolerance curve in a diabetic patient, fasting blood-sugar, 120 mg. per 100 c.c.

glucose tolerance test is required whether or not glycosuria be present (Figs 383–385). A high fasting blood-sugar (180 mg. per 100 c.c. or more) in itself establishes the diagnosis of diabetes.

The following cases, one of which has previously been reported,[2] illustrates the danger of basing a diagnosis upon the presence of glycosuria alone, without blood-sugar estimations:

Case I.—A girl, eighteen years of age, was sent to the Cleveland Clinic July 27, 1921, with the history that she had been well until the preceding summer, when she noticed progressive weakness and loss of appetite She was examined by her physician, who found sugar in the urine, and immediately put her on the so-called "Allen treatment" for diabetes, with the result that in about four months her weight dropped from 123 to 63 pounds (55 79–28 57 kg) During most of this period sugar was present in the urine Her family history was negative She had not menstruated for eighteen months There had been no previous illnesses She had had a tonsillectomy three years before

Physical examination showed the patient to be moderately developed, but markedly emaciated, with a dry, ichthyotic skin, otherwise the physical findings were negative

The laboratory findings were as follows. The Wassermann reaction was negative Blood examination revealed Red blood-count, 3,590,000; white blood count, 9400, hemoglobin, 65 per cent , differential count polymorphonuclears, 82 per cent , basophils, 1 per cent , small lymphocytes, 17 per cent Urine examination revealed the presence of sugar, otherwise it was negative. Phenolsulphonephthalein functional kidney test showed the excretion of 55 per cent the first hour and 15 per cent the second Blood chlorids amounted to 522 mg per 100 c c A glucose tolerance test made on July 28th gave a normal blood-sugar curve

In this case, as stated above, the condition had been diagnosed as diabetes mellitus by the patient's physician on the basis that she had sugar in the urine On this basis she had been put on a rigidly restricted diet and kept on it until she had lost almost 50 per cent of her weight, but she still showed sugar in the urine Our examination revealed that she had a normal blood-sugar content, and her ability to utilize carbohydrates—the glucose tolerance test—was demonstrated to be normal by the perfectly normal curve; that is, she was able to utilize all the carbohydrates one could give her. This was strikingly demonstrated in the hospital later on, when a heavy carbohydrate diet, high in calories as well, failed at any time to bring her blood-sugar above the normal level Within six weeks she had regained more than her normal weight A blood-sugar examination made one year later showed her blood-sugar to be still normal

Case II.—A boy of seventeen with the following history came to the Cleveland Clinic on March 26, 1923. After a bad cold with a sinus infection sugar had been found in his urine He had been put on a rigid diabetic diet,

to which he did not adhere There had been no loss of weight, no thirst, and no nocturia. He had attended school regularly. Although sugar had repeatedly been found in the urine, blood-sugar estimations had never been made There was no history of diabetes in the family. He had had measles, whooping-cough, and chickenpox a year before, and mumps at the age of twelve. A tonsillectomy and adenectomy had been performed when he was six years old.

On admission to the Clinic his urine was found to have a specific gravity of 1030 and to contain 3 plus sugar. The blood-sugar content was 89 mg. per 100 c.c. The Wassermann was negative

Because of the insufficient urine and blood-sugar data a glucose tolerance test was done the next day, with the following results·

	Fasting	Glucose by mouth, gm	One-half hour after	One hour after.	Two hours after	Three hours after	Four hours after
Blood-sugar mg per 100 c.c.	84	100	113	84	98	79	84
Urine sugar	0	0	0	0	0	0	0

These findings give a normal curve, thus ruling out diabetes The presence of sugar in the urine is explained by a low renal threshold which, however, is at a blood-sugar level above 113 mg per 100 c c , as no sugar was found at this concentration

All that saved this boy from the unfortunate effects experienced by the patient whose case was cited above, was the fact that he failed to carry out the dietary restrictions prescribed

The fact that glycosuria appears in the urine only when the blood-sugar level is above the point of renal permeability has led to some confusion in every-day practice. Let us suppose that in 2 patients the urinary and blood-sugar findings are as follows:

	Renal permeability, mg per 100 c c.		Blood-sugar, mg. per 100 c c.	Sugar in the urine
Case I	240		180	3 plus
		Two hours later .	230	neg
Case II	240		220	neg.
		Two hours later . .	200	plus

In one case when the blood-sugar content is 180 mg. per 100 c.c., much lower than the point of renal permeability, we find a large quantity of sugar in the urine. Later, in the same

patient, when the sugar content is at 230 mg. per 100 c.c., there is no sugar in the urine.

In the second case, when the blood-sugar content is 220 mg. per 100 c c , there is no sugar in the urine, whereas later, when the blood-sugar content has fallen to 200 mg. per 100 c c., glycosuria is present

Figure 386 explains this apparent discrepancy. In the interpretation of glycosuria we must always take into consideration

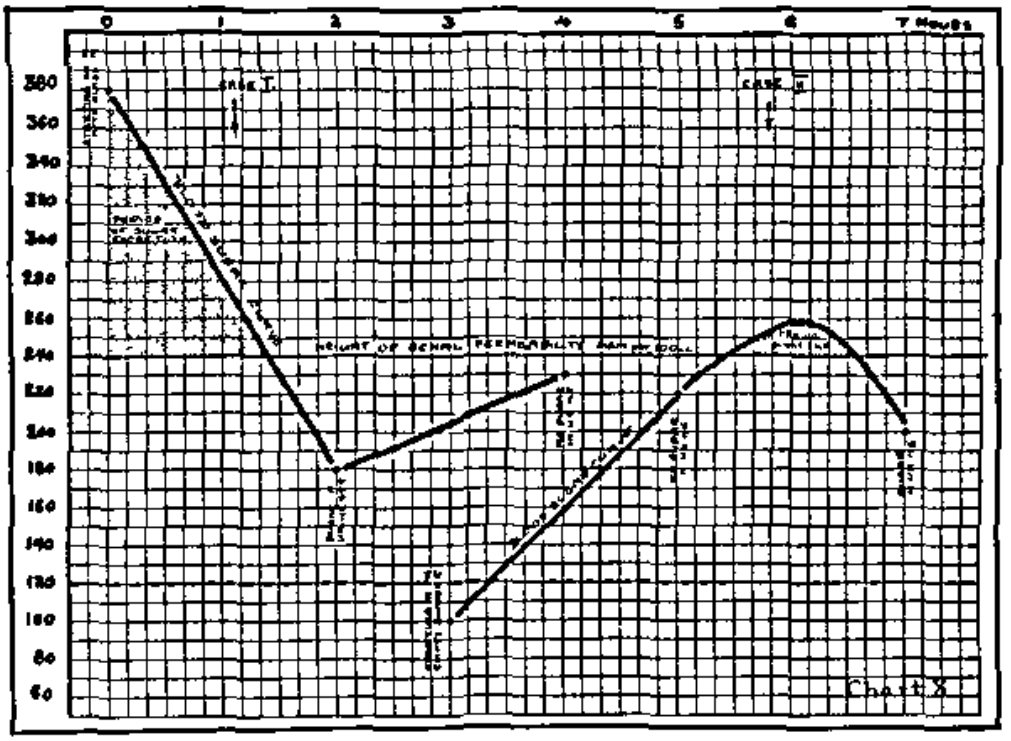

Fig 386 —Chart of two hypothetic cases illustrating certain possible variations in the relation of the urine sugar to the blood-sugar

the blood-sugar content not only at the time of the urinary examination but also during the time which has elapsed since the last voiding of urine If the blood-sugar content at any time since the last voiding is above the point of renal permeability, sugar is excreted into the urine, and even though the blood-sugar level may be below the point of renal permeability at the time of the urine examination, nevertheless, since the urine examined represents that which has collected since the last voiding, during a part of which time the blood-sugar level was above the point of renal permeability, it will contain sugar.

Another point which should be noted in regard to the urine examination is the fact that the specific gravity is not a criterion of the presence of glycosuria.[3]

To establish this point I analyzed 1000 specimens of urine to discover the relationship, if any, between the sugar content and the specific gravity, with the following results:

Specific gravity	1000 to 1005	1006 to 1010	1011 to 1015	1016 to 1020	1021 to 1025	1026 to 1030	Total number of cases.
Glycosuria present in	79 27%	71 46%	58 58%	68 52%	79 70%	171 85%	526
Glycosuria not present in	216 73%	84 54%	43 42%	61 58%	33 30%	37 15%	474
Total	295	155	101	129	112	208	

This table shows very definitely that urine of very low specific gravity may contain sugar, and that, on the other hand,

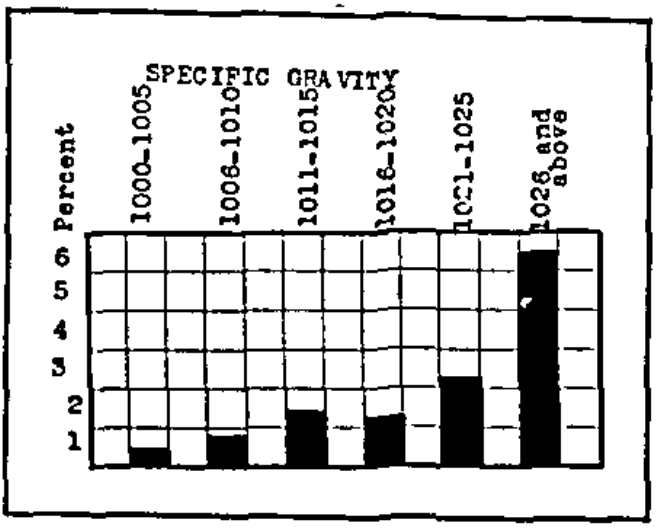

Fig 387.—Average percentage of urine sugar at different specific gravity levels in 268 diabetic cases

urine of very high specific gravity may contain no sugar. (Figs. 387, 388 and Table 1.)

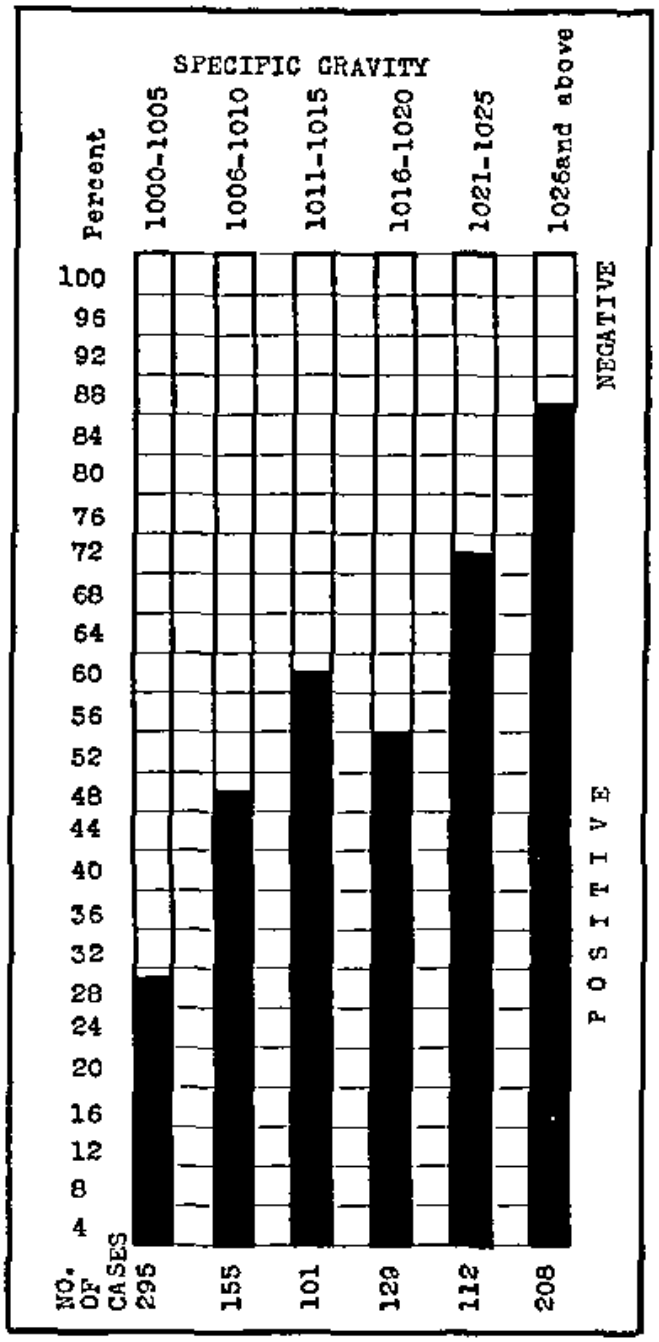

Fig 388 —The relation of specific gravity to urine in 1000 cases

TREATMENT

The treatment of diabetes consists in carefully balancing the food intake with the available internal secretion of the pancreas. The daily diet of a normal person doing light work consists of about 400 gm of carbohydrates, 75 gm of proteins, 75 gm of fats, a total of about 2500 calories The glucose content of the proteins is about 58 per cent , and of the fats about 10

TABLE I

PERCENT OF URINE SUGAR AT DIFFERENT SPECIFIC GRAVITY LEVELS IN 268 CASES

Specific Gravity	1000 1005	1006 1010	1011 1015	1016 1020	1021 1025	1026 1030	1030 and above	
Percent of Sugar in the Urine	.13	.16	.33	.29	.40	.65	3.40	1.00
	.08	.15	.10	.30	.31	2.00	1.50	2.50
	1.10	.11	.38	.31	.70	2.00	1.00	.14
	.42	.42	.09	.14	1.80	2.00	2.50	1.30
	.11	.77	1.80	.91	.65	1.20	2.10	1.30
	.65	1.30	1.80	1.10	1.90	1.70	3.60	1.30
	.38	.33	1.20	1.70	1.20	3.60	2.20	2.00
	.01	.12	1.90	.40	2.60	3.00	2.9 0	2.50
	.63	1.30	2.10	1.20	3.30	.38	4.00	2.50
	.42	1.40	1.90	.31	2.20	1.80	3.80	2.50
	.21	1.10	.65	1.10	.45	2.30	3.10	2.50
	.48	1.30	2.20	2.40	2.30	2.10	3.60	6.25
	.55	1.00	1.10	.48	.38	2.60	4.00	7.15
	1.30	1.10	2.00	1.80	3.29	.91	5.00	8.33
	.33	1.70	1.90	.91	3.60	2.20	1.28	5.55
	.33	.67	1.40	.28	3.00	2.70	1.67	5.55
	.67	.91	1.10	2.40	2.60	3.40	.83	
	.14	1.20	2.10	.30	3.70	3.60	.34	
		1.10	2.40	.10		3.60	.14	
		.43	1.30	1.30	.68	3.60	.68	
		.43	1.80	1.80	1.40	3.60	.33	
		.91	1.80	1.70	1.60	1.90	.69	
		.11	.71	1.90	1.60	3.10	1.50	
		.13	1.90	2.40	3.10	2.80	1.40	
		.25	1.90	2.90	1.90	3.20	1.30	
		.40	1.40	2.10	1.20	3.30	1.60	
		.63	.34	2.10	1.00	1.30	4.16	
		1.17	.38	.61	1.70	1.50	4.16	
		2.10	.33	.63	2.00	3.10	1.30	
		.37		.71	2.30	.36	2.94	
		.63		.10	2.40	2.40	7.69	
		.58		.58	3.00	2.40	4.90	
		.58		4.35	3.19	3.80	2.10	
					3.60	2.80	6.25	
					2.40	2.80	7.35	
					3.70	4.00	3.30	
					1.90	1.90	2.50	
					2.50	2.20	2.00	
					3.80	2.00	2.00	
					3.30	2.20	2.00	
					2.90	2.20	.88	
					4.30	3.00	2.90	
					1.30	5.00	.27	
					1.40	2.20	4.30	
					1.70	1.50	4.30	
						2.40	1.70	
						2.40	.20	
						2.30	.91	
Average Percent	.46	.78	1.34	1.19	2.11	5.37		

per cent. About 1 gram of protein per kilo of body weight is required to maintain the nitrogen equilibrium. Thus a person weighing 125 pounds (56 kg.) would require 56 gm. of protein each twenty-four hours. Protein itself has a high specific dynamic action, so that some authorities think it advisable to give as little protein as possible. Since the carbohydrate metabolism in a diabetic patient is weakened, the carbohydrate intake must necessarily be markedly reduced. Since, as stated above, the glucose content of fat is only 10 per cent., it is the least objection-

able agent, and it is on this principle that Newburgh and Marsh have based their conclusion that large amounts of fat should be included in the diabetic diet

When Allen introduced his principle of undernutrition in the treatment of diabetes his purpose was to spare the weakened function of the pancreas and, therefore, to this end he made a very rigid restriction in the diet He considered that in diabetes not only is the ability to utilize carbohydrates impaired, but the metabolism as a whole is weakened also. He limited the fats on the principle that fat is not properly oxidized if a sufficient amount of carbohydrate is not oxidized also. As it is popularly expressed, "fat burns in the flame of carbohydrates"; if this flame is meager, fat does not burn properly, and consequently such by-products as the fatty acids—acetone, diacetic acid, and beta-oxybutyric acid—are produced in excess, with resultant acidosis, leading to a coma In the past this danger was the sword of Damocles which hung over the heads of physicians who were treating diabetes. Newburgh and Marsh then gave the diabetic more food containing a large proportion of fat, seemingly without embarrassing his weakened metabolism. Contrary to the views of Allen, their work would suggest that the available carbohydrate in the diet of a diabetic patient is alone at fault. However, the data which they offer are still limited, and it will not be until comparative data of series of diabetic patients on high fat diets and on moderate undernutrition diets have accumulated over a long period of time that we shall be able to draw final conclusions

The question naturally arises as to how much fat can be used. My criterion for the safe use of fats has been the test of the blood-plasma for acetone If the organism is not burning the fats properly, fatty acids are liberated which circulate in the blood-stream and can be detected by the simple Wishart test If the amount of these acids increases from day to day the fat intake should be reduced until the proper balance is established. The presence of acetone in the urine is not a criterion, for the important point, it seems to me, is not how much acetone is excreted, but how much is concentrated and

held back by the blood-stream. It is the acetone in the plasma which brings on acidosis and coma, not the acetone which has been discarded by the organism into the urine.

Thus by allowing a patient 1 gram of protein per kilo of body weight his nitrogen metabolism is taken care of, and by allowing him as much fat as possible the total number of needed calories are supplied.

In order to determine the tolerance of the individual patient I first bring the blood-sugar down to normal by putting the patient for two or three days on a very low diet containing approximately 30 grams of carbohydrates, 30 grams of proteins, and 40 grams of fat—a total of 600 calories

As soon as the blood-sugar is normal the diet is gradually increased to 60 gm. of carbohydrates, 50 gm. of proteins, and enough fat to make a total of 1000 calories. After two or three days the diet is again increased to about 65 gm. of carbohydrates, 50 gm. of proteins, and enough fat to make a total of 1400 calories. If after several days the blood-sugar remains normal, the diet is increased to 70 gm. of carbohydrates, 50 gm. of proteins, and enough fat to make a total of 1600 calories; 50 to 60 gm. of proteins are sufficient for the average patient; the carbohydrates are increased gradually, the fat more rapidly.

In this way the progress of each patient is checked from day to day, and it is possible to determine in each case whether the diet may be increased rapidly, or whether the increase must be very gradual. There is no set rule of procedure in these cases. Each case is an unknown problem and must be studied as such.

This procedure, however, consumes a con.iderable period of time. I have, therefore, adopted the following method which will be described in detail later: Upon entrance to the hospital the patient is put on a diet of 100 gm. of carbohydrates, 60 gm. of proteins, and 128 gm. of fat—a total of 128 calories. Insulin is administered until the blood-sugar reaches normal, when it is discontinued or given in very small doses. This procedure not only saves time but also puts the patient on a diet sufficiently high in calories to keep him contented. It also gives him the

same definite diet during his stay in the hospital, so that automatically the proportions and the kind of food he may eat are more or less impressed upon his mind. Changing the diet every few days defeats this object.

If it is found that the pancreatic function of the patient will not tolerate this diet, insulin is used. The method of determining the amount of insulin necessary in each case is discussed later in the paper.

Urinary examinations are made systematically that the records of each case may be complete, but I consider that they are unimportant, for, as has been stated above, glycosuria tells only a very small part of the story, and is of value only as a signpost to indicate the need for blood-sugar estimations. However, I think it is a good plan to teach the patient to make urinary examinations, for these will warn him when his blood-sugar rises above the point of renal permeability, so that he may promptly present himself for blood-sugar estimations The most important point is that the specimen to be examined be a twenty-four-hour specimen in order to determine the total output of sugar. If recourse to the blood examination is impossible, the diet can be adjusted according to these findings

Patients whose glucose tolerance is low should have weekly blood-sugar examinations, once in two weeks, once a month, or once in three months may be sufficient in other cases. Only the physician in charge can decide as to the time which may be allowed to elapse between blood-sugar estimations

Clinically, I think that we can group all diabetic patients into one of two distinct classes. (1) those whose tolerance under treatment and proper diet remains stationary, and (2) those whose tolerance under treatment and proper diet continues to increase The explanation which I have advanced is that the patients in the first group have what may be termed an "anatomic type" of diabetes, that is, in these cases we have to deal with an actual destruction of the islands of Langerhans. *In the second group, on the other hand, we are dealing with functional* changes In these cases, if they are controlled by proper diet, the normal function of the pancreas will be partially

restored and clinical improvement will follow These two groups may be subdivided as follows:

A. *Anatomic type*, in which there is no increased tolerance under treatment, but no downward progress if properly controlled	1. *Total diabetes*, in which all insular tissue is destroyed, so that no carbohydrates are utilized, and even the 58 per cent. of proteins and 10 per cent of fat are converted into sugar and excreted
	2. *Milder cases*, in which there is a partial destruction of the insular tissue
	3 *Mild cases*, in which there is only a slight destruction of insular tissue
B *Functional type*, in which definite clinical treatment is followed by improvement and a gain in tolerance.	1 *Very severe cases*, in which there is a marked functional derangement of insular tissue, in which, however, the function is largely restored by proper diet and control.
	2 *Severe cases*, in which there is considerable functional derangement, with a comparatively quick return to a fair tolerance under treatment
	3. *Mild cases*, in which there is a mild functional derangement, treatment being followed by almost complete restoration of normal function

Tables 2 to 8 illustrate the progress of 7 diabetic patients under the dietary regimen described above, the blood-sugar remaining normal and their tolerance for carbohydrates increasing.

In order that these patients may continue to follow this dietary regimen it is necessary that during their stay in the hospital—usually not more than two weeks—they be taught how to select their food so as to include the proper amounts of proteins, fats, and carbohydrates. From ten to fourteen days is a very short period in which to learn the necessary dietetic principles, but it is essential for the ultimate welfare of the patient that we make the time count. Modern diabetic hospitals are

TABLE 2

Date	Blood Sugar mg. per 100 cc.	Urine Sugar	Diet C	P	F	Calories
7/14/22	333	+++	75	40	15	600
7/17/22	333	2/5%	15	20	40	500
7/20/22	265		15	20	40	600
7/24/22	191		15	20	60	900
7/26/22	147		15	25	93	1000
7/31/22	124		35	40	133	1500
8/4/22	130		30	40	135	1500
8/11/22	108		40	50	182	2000
8/18/22	106		50	60	228	2500
8/25/22	121		75	75	211	2500
9/14/22	104		80	80	217	2600
10/12/22	107		80	80	217	2600
11/14/22	100	0	80	80	217	2600
12/14/22	108		90	80	213	2600
1/16/23	157		90	75	182	2400
2/12/23	102	0	90	85	200	2500
3/12/23	111	0	100	85	195	2500
6/5/23	96		100	85	195	2500

TABLE 3

Date	Blood Sugar mg. per 100 cc.	Urine Sugar	Diet C	P	F	Calories
2/28/22	262					
3/4/22	111	0	15	20	40	500
3/8/22	102		40	40	97	1000
3/10/22	130		40	40	97	1200
3/13/22	113		25	35	84	1000
3/16/22	122		35	40	77	1000
3/20/22	78		Liberal Diet			
3/25/22	66		"		"	
3/30/24	105		"		"	
4/3/22	105		"		"	
5/13/22	104		"		"	
7/14/22	121		"		"	
12/1/22	118	0	"		"	
5/31/23	139		"		"	
7/20/23	108	0	"		"	

rather diabetic schools, where the patient goes not only to be straightened out, but also to learn how to carry on that which helped him while he was in the hospital. Diabetes is a patient's problem, not a doctor's problem. A physician is the consultant who suggests and directs, but the patient himself is his own physician, and the final responsibility is his He must be taught not only dietetics but also how to look out for infections, and what to do when they occur. The best clinical result can be quickly spoiled by a cold which is not properly taken care of. This the patient must fully realize.

Many patients whose cases are mild in time regain a great deal of their normal tolerance, so that a simple restriction of carbohydrates by cutting out sugar and pastry from the diet

TABLE 4

Date	Blood Sugar mg. per 100 cc.	Urine Sugar	Diet C	P	F	Calories
9/3/21	288	++				
9/17/21	230		20	40	51	700
9/26/21	104	0	40	50	71	1000
9/30/21	75		50	60	84	1200
10/4/21	88	0	65	70	117	1600
10/7/21	104		80	70	155	2000
10/29/21	207	0	80	70	155	2000
10/31/21	105			Liberal Diet		
11/25/21	98	0		"		"
12/24/21	142			"		"
1/14/22	125			"		"
2/11/22	98			"		"
4/1/22	112			"		"
4/15/22	91			"		"
5/6/22	111	0		"		"
9/16/22	163			"		"
10/28/22	107			"		"
12/9/22	113			"		"
1/13/23	105			"		"
4/14/23	201	0		"		"
4/16/23	155			"		"
8/22/23	133			"		"

TABLE 5

Date	Blood Sugar mg. per 100 cc.	Urine Sugar	Diet C	P	F	Calories
4/18/22	174		15	20	40	500
4/22/22	176		15	20	40	500
4/24/22	152		15	20	40	500
4/27/22	170		15	20	40	500
4/29/22	192		15	20	40	500
5/2/22	200		15	20	40	500
5/8/22	186		15	20	40	500
5/11/22	174		20	35	64	800
5/15/22	158		20	35	64	800
5/19/22	142		20	35	64	800
5/23/22	130		20	35	64	800
5/27/22	124		25	40	82	1000
5/31/22	120		30	50	108	1300
6/7/22	112		45	60	175	2000
7/15/22	155		45	60	175	2000
9/2/22	124			Liberal Diet		
10/2/22	125			"		"
11/13/22	113			"		"
1/20/23	121	0		"		"
4/5/23	133	0		"		"
8/2/23	104					
10/4/23	100	0		"		"

and using starchy foods in moderation is sufficient. The following case illustrates this point:

A young college student, eighteen years of age, from the northwestern part of Canada, came to the Clinic in April, 1922, for the treatment of diabetes, which had been discovered five months before in the course of an examination for life insurance, when sugar had been found in the urine He had not had thirst, polyuria, or polyphagia at any time. A rigid diet had been prescribed, but, due to a misunderstanding, he had not adhered to it very faithfully.

He had had measles, grippe, and pneumonia in childhood, and some sort

TABLE 6

Date	Blood Sugar mg. per 100 cc.	Urine Sugar	Diet C.	P	F	Calories
8/15/22	638	3.3%	15	20	40	500
8/19/22	294		15	20	40	500
8/22/22	204		15	20	40	500
8/26/22	137		25	45	68	900
8/28/22	267	++	15	20	40	500
9/1/22	88	0	35	55	71	1000
9/5/22	103	0	45	60	86	1200
9/9/22	137	0	35	55	71	1000
9/12/22	97	0	40	55	91	1200
9/16/22	178	0	35	55	71	1000
9/20/22	106		40	55	91	1200
9/23/22	148		35	55	71	1000
9/27/22	254	+	15	20	40	500
9/30/22	250	0	15	20	40	500
10/ 3/22	111		25	35	62	800
11/21/22	110		135	55	65	1350
12/2/22	109		140	55	80	1500
12/30/22	96		145	60	69	1520
1/20/23	97	0	152	60	74	1520
2/2/23	120		152	60	74	1520
3/3/23	113	0	152	60	74	1520
3/14/23	106	0	152	60	74	1520
5/12/23	120	0	180	80	95	1900
6/9/23	86		180	80	106	2000
7/10/23	109	0	"	"	"	"
7/23/23	131	0	"	"	"	"
7/28/23	117	0	"	"	"	"
7/31/23	115	0	"	"	"	"
8/29/23	119		"	"	"	"

TABLE 7

Date	Blood Sugar mg. per 100 cc.	Urine Sugar	Diet C	P	F	Calories
5/19/21	224	++	15	15		250
5/23/21	117	0	40	60	66	1000
5/26/21	98	0	60	70	75	1200
5/31/21	123		60	70	75	1200
6/ 4/21	86		60	70	75	1200
6/ 9/21	122	0	80	70	77	1300
6/11/21	124	0	80	70	77	1300
9/ 8/21	120		80	70	77	1300
1/10/22	110			Liberal diet		
3/22/22	83	0		"		
5/9/22	129			"		
10/18/22	150			"		
5/15/23	150			"		
10/10/23	199			"		
12/19/23	125					

TABLE 8

Date	Blood Sugar mg. per 100 cc.	Urine Sugar	Diet C	P	F	Calories
1/11/22		++	10	10	25	400
1/12/22	350					
1/13/22		+++	15	10	40	500
1/14/22	182	+++	15	10	40	500
1/18/22	118		25	20	68	800
1/20/22	118	0	25	20	68	800
1/23/22	100		25	35	84	1000
2/15/22	250		40	30	102	1200
2/22/22	160		50	40	137	1600
3/6/22	193		50	40	137	1600
3/16/22	158		60	40	155	1800
4/1/22	116		100	60	151	2000
4/15/22	86			Liberal diet		
4/29/22	88			"		
4/26/22	104			"		
11/25/22	107	0		"		
2/10/23	110	0		"		

of kidney trouble and brain fever as a baby. In March, 1920 an attack of scarlet fever was followed by a swelling of the tonsils, from which pus could be expressed. The following August tonsillectomy was performed

The general physical examination was negative.

His blood-sugar on admission was 200 mg per 100 c c.; no acetone was present in the plasma. The laboratory findings were as follows. glycosuria; plasma chlorids, 615, blood urea, 21, blood uric acid, 3, blood creatinin, 1 4, and non-protein-nitrogen, 24 mg. per 100 c c. The Wassermann test was negative. The phenolsulphonephthalein kidney functional test showed an excretion of 45 per cent. during the first hour and 15 per cent. during the second hour. A glucose tolerance test a few days later gave the following results· blood-sugar before the ingestion of 100 gm. of glucose, 130, one-half hour later, 156, one hour later, 174, two hours later, 265, three hours later, 294; four hours later, 288 mg per 100 c c. Sugar was present in the urine at the end of two-, three-, and four-hour periods

The following diet was prescribed: 15 gm of carbohydrates, 20 gm of proteins, 40 gm. of fat—a total of 500 calories per day. In three days the blood-sugar had dropped to the normal content and his diet was increased to 20 gm. of carbohydrates, 35 gm. of proteins, 75 gm of fat—a total of 900 calories During the seventh week the diet was increased to 35 gm of carbohydrates, 40 gm. of proteins, and 111 gm. of fat—a total of 1300 calories, the blood-sugar remaining at the normal level with the exception of the last few days in the hospital, when it was somewhat increased, probably because of anxiety and worry.

Since the patient lived several hundred miles from any chemical laboratories, he was taught the routine method of chemical blood examination, and returned home with the essential equipment for making his own blood-sugar tests. A month later he reported that his blood-sugar was remaining at the normal level on a diet of 45 gm. of carbohydrates, 55 gm of proteins, 150 gm of fat, a total of 1750 calories Within three months from the time he returned home his diet had been increased to 130 gm of carbohydrates, 80 gm. of proteins, and 170 gm of fat, a total of 2370 calories, with his blood-sugar still remaining normal. He was also gaining in weight and was able to carry on all the activities of a normal boy. Moreover, he was assisting his father, a physician, by making blood-sugar estimations for other diabetic cases

This seems to have been one of the cases belonging in Type B, Group 4, as described in the suggested classification on page 1017, the diabetic condition apparently being due to an early functional derangement of the pancreas occasioned by the infectious diseases during childhood. I could cite several other cases in each of which a like recovery has taken place as the result of the patient's understanding of and adherence to instructions, and the result in each case has been accomplished without insulin.

The routine of diabetic treatment has not changed with the discovery of insulin, for controlled diet is still the "sine qua non." What, then, is the function of insulin in the treatment of diabetes? Insulin is an extract of the islands of Langerhans containing the essential product of that part of the pancreas which makes possible the utilization of carbohydrates Therefore by the administration of insulin the glucose tolerance of the patient is increased so that an additional amount of carbohydrates can be included in his diet. Tables 9 to 11 show the diets given in 3 cases in which insulin was used. Wilder, of the Mayo Clinic, says, "what insulin does is to insure a definite increase in tolerance while it is being used."[4] In younger patients insulin seems to produce some actual restoration of the cells

TABLE 9

Date	Blood Sugar mg. per 100 cc.	Urine Sugar gm/24 hr.	Diet C	P	F	Calories	Insulin units		Remarks
11/20/22	270	1.5	25	35	54	750	32		Admitted
11/21/22	222		25	35	54	750	64		to hos-
11/22/22	165		25	35	54	750	16		pital
11/23/22	192		25	35	54	750	16		
11/24/22	173		15	20	40	500			
11/25/22	192	3.98	15	20	40	500			
11/26/22	176	4.27	35	40	77	1000			
11/27/22	200	9.78	35	40	77	1000			
11/28/22	218	10.23	35	40	77	1000	40		
11/29/22	204	2.75	15	20	67	750			
11/30/22		9.72	15	20	67	750			
12/1/22		7.24	15	20	67	750			
12/2/22	184	3.43	10	15	22	300			
12/3/22		1.67	15	20	40	500			
12/4/22	155	1.87	15	20	40	500			
12/5/22		1.82	15	20	67	750			
12/6/22	154	1.2	20	30	84	1000			
12/7/22			20	30	84	1000			
12/8/22		1.57	20	30	84	1000			
12/9/22	130	1.	20	30	84	1000			
12/10/22			20	30	84	1000			
12/11/22	125		20	30	111	1200			
12/21/22	139		20	30	111	1200			Discharge
1/2/23	145		20	30	111	1200			from hos-
1/15/23	127		25	30	142	1500			pital
2/1/23	136		25	35	140	1500			
2/14/23	128	neg.	35	35	135	1500			
2/28/23	143	neg.	40	40	130	1500			
3/14/23	190		40	40	130	1500			
3/28/23	208		35	35	80	1000			
4/6/23	165	neg.	35	35	102	1200			
4/20/23	170	neg.	35	35	102	1200			
5/5/23	161		35	35	135	1500			
6/1/23	199		35	35	135	1500			at home
7/5/23	248	tr.	35	35	135	1500	20	20	units/
7/20/23	126		45	40	162	1800	10	10	" "
8/1/23	155	neg.	45	40	162	1800	20	20	" "
8/6/23	189		45	40	162	1800	20	20	" "
8/15/23	128	neg.	50	45	157	1800	20	20	" "
8/24/23	185	tr.	50	45	157	1800	20	20	" "
9/5/23	161	neg.	50	45	157	1800		20	" "
9/29/23	201	++	50	45	157	1800		20	" "
10/12/23	185	neg.	60	50	175	2000		20	" "

TABLE 10

Date	Blood Sugar mg. per 100 cc.	Urine Sugar	Diet C	P	F	Calories	Insulin	Remarks
8/20/23	353	3.2						
8/22/23			30	30	40	600		Admitted
8/23/23	176	0	30	30	40	600	10	to hospi-
8/24/23	177	+	50	50	100	1300		tal
8/24/23	164	0	50	50	100	1300	9	
8/25/23		tr.	50	50	100	1200		
8/27/23	118	tr.	60	50	128	1600		
8/28/24	141	0	60	50	128	1600		
8/29/23	108	0	80	50	142	1800		
8/30/23	84		80	50	142	1800		
8/31/23	125		80	50	142	1800		
9/1/23	130		80	50	142	1800		
9/2/23		tr.	80	50	142	1800		
9/3/23		0	80	50	142	1800		
9/4/23	122		80	50	142	1800		
9/5/23	129		90	60	155	2000		
9/6/23	134		90	60	155	2000		
9/7/23	145		90	60	155	2000		Discharged
9/28/23	117	tr.	90	60	155	2000		from hos-
10/12/23	133		90	60	155	2000		pital

TABLE 11

Date	Blood Sugar mg. per 100 cc.	Urine Sugar	Diet C	P	F	Calories	Insulin	Remarks
8/10/23	600	5.5	30	30	40	600		Entered
8/11/23	201		30	30	40	600	5	hospi-
8/12/23	152	1.4	50	40	61	1000	5	tal
8/13/23	149		80	40	61	1000	5	
8/14/23	114		60	50	116	1600	10	
8/15/23	133	1.0	60	50	116	1600	10	
8/16/23			60	50	116	1600		
8/17/23	111		60	50	116	1600	10	
8/18/23	130		65	60	153	2000	10	
8/19/23	110	.5	65	60	153	2000	7	
8/20/23	129		65	60	153	2000		
8/21/23	122		65	60	153	2000		
8/22-23	92		65	60	150	2000		
9/19/23	117		75	60	162	2000		Dis-
								charged
								from
								hospi-
								tal

In order to study the effects of insulin on the blood-sugar curve I made comparative studies of the effect on the blood-sugar curve of low diets and of low diets plus insulin[5] (Figs. 389–392). These studies have been published in detail. In each chart the solid black line shows the variations during one day in the blood-sugar of a diabetic patient as determined by hourly estimations. Each of these patients was on a diet with a low caloric value. After each meal, even with the small carbohydrate intake, there is a definite rise of blood-sugar and a prolonged hyperglycemia.

In order to determine the effect, if any, of insulin upon the postprandial hyperglycemia, the same routine was carried out

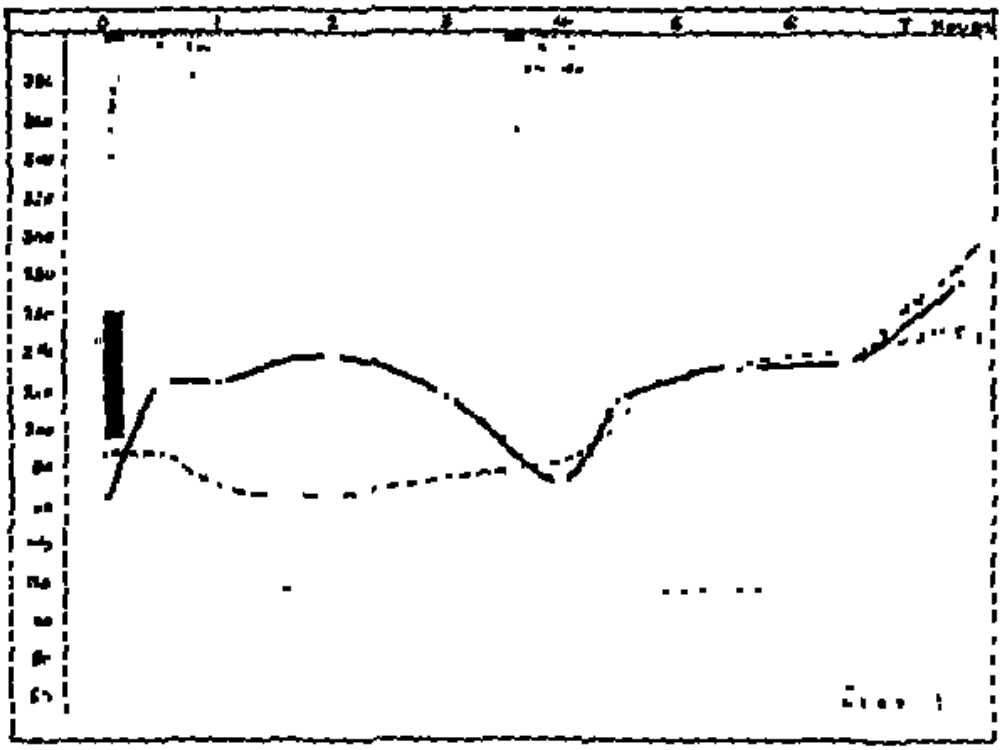

Fig 389.—Comparison of the blood-sugar curves of diabetic patient on two successive days without and with insulin respectively

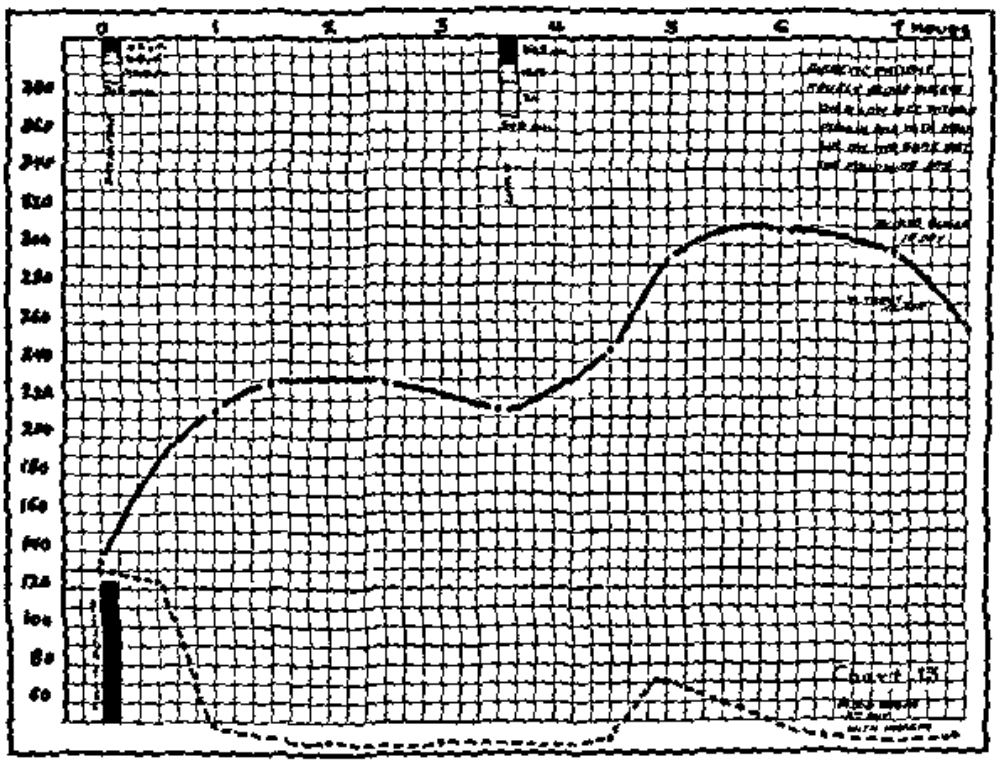

Fig 390.—Comparison of the blood-sugar curves of diabetic patient on two successive days without and with insulin respectively.

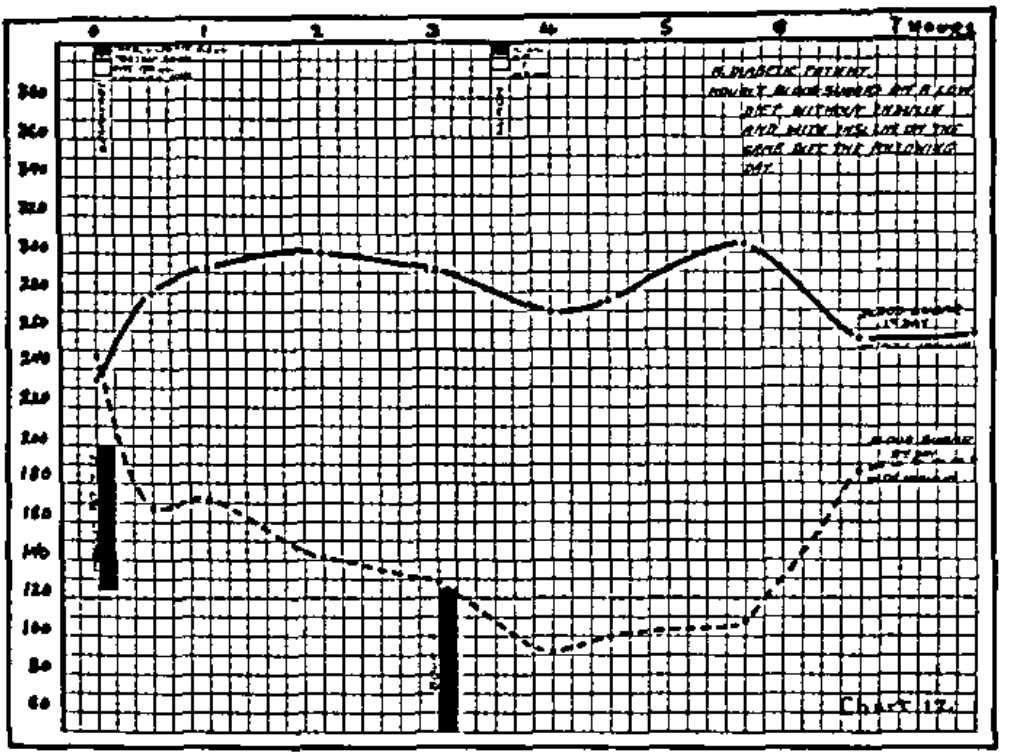

Fig. 391.—Comparison of the blood-sugar curves of diabetic patient on two successive days without and with insulin respectively

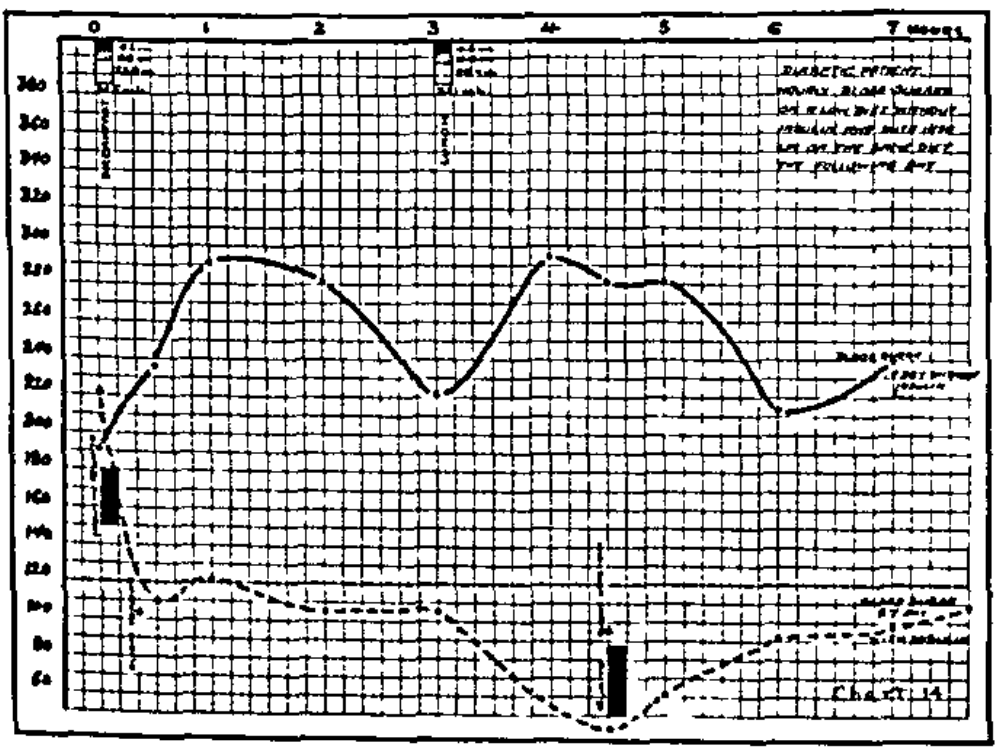

Fig. 392.—Comparison of the blood-sugar curves of diabetic patient on two successive days without and with insulin respectively.

the following day, with the addition of one or more doses of insulin, as noted. The effect of insulin on the blood-sugar curve is shown on each chart by a heavy broken line The response to insulin is evident in every case by the depression of the blood-sugar curve, but this response varies a great deal in the different individuals Because of this variation it has been impossible to standardize the insulin dosage, as Allen has pointed out, and therefore each case becomes a separate experimental study as far as the required dosage of insulin is concerned. Once the effects in the individual case have been determined, however, the plan of treatment for that case can be established

To determine the amount of insulin to be used in a given case either of the following methods may be used:

The patient may be placed in the hospital and his blood-sugar reduced to the normal level by a low diet, after which the diet may be gradually increased until the actual tolerance of the patient is ascertained If this tolerance should not be sufficent to take care of the amount of food necessary for the maintienance of that patient—usually about 100 gm of carbohydrates, 70 gm of proteins, and fat to make a total of 2000 calories—then by repeated trials we find out how much insulin is required to take care of this additional food and at the same time maintain a normal blood-sugar curve Such a routine requires time and necessarily is expensive to the patient, so that any short cut which may shorten the stay in the hospital is of distinct advantage.

For this reason I administer insulin as soon as the patient reaches the hospital in order that the blood-sugar may be reduced to the normal level as soon as possible His actual tolerance is then established as outlined above.

Insulin may be administered either intravenously or hypodermically. When given intravenously, naturally it acts more quickly and its administration may be followed immediately by a meal. If given hypodermically it should be administered from twenty to thirty minutes before a meal

My own practice is to inject the insulin into the vein through the same needle as that used for taking blood for sugar esti-

mation, that is, I inject the insulin, then, leaving the needle in place, I rinse out the syringe with blood which is passed back into the vein, after which 1½ c.c. of blood is withdrawn Thus, with minimum discomfort to the patient, I obtain information as to his blood-sugar from day to day while the patient is in the hospital and receiving varying doses of insulin, until the dosage needed in his individual case is established. In cases in which still more specific information is required in addition to the above procedures, blood-sugar estimations are made one or more hours after each insulin injection.

Much has been written regarding the reactions which may follow the administration of insulin. Thus, for example, Graham says: "When blood-sugar falls to 0 070 per cent symptoms develop, and if it falls to 0.035 per cent. the patient becomes unconscious." Some men say that death occurs when the blood-sugar reaches 0.040 per cent., but I have given thousands of intravenous doses of insulin, in some cases repeating a dose of 100 units two or three times a day, and I have seen very few reactions. When insulin first came into use, I made a special study of these reactions, and in no case did I find it necessary to use emergency measures, although in some cases hypoglycemias were as low as 17 and 18 mg. per 100 c.c. In the hospital the nurses have a standing order to give 5 c.c. of whisky with 1 teaspoonful of sugar in ½ glass of hot water if a reaction occurs. This restores a patient almost immediately, and in our experience it has never been necessary to repeat such a dose. Reactions from insulin can also be combated by taking the juice of one orange, or sugar, or carbohydrate in any form, by mouth. In patients who are unconscious a 5 to 10 per cent. solution of glucose given intravenously is the best restorative measure. Recently Eli Lilly & Co. have put on the market sterile ampules of 10 gm. of dextrose in 20 c.c. of water, which make an ever-ready means of restoration in these emergencies. Barborka[8] makes the statement that "only glucose of the greatest purity should be employed, dissolved in freshly distilled water, and administered with all the precautions necessary in making intravenous injection." It should be borne in mind, however,

that glucose of the highest purity is secured by precipitation with acetic acid, the remaining traces of which will cause reactions at times, as was shown in a large series of pneumonia cases in the treatment of which I used glucose intravenously.[7] It is better, therefore, to use the commercial glucose. The solution should be filtered so as to exclude any grosser impurities; it should also be sterilized and given warm.

Coma is a complication of diabetes which arises either in neglected cases or in cases which have been under treatment as the result of an infection or of some indiscretion in eating, with resultant pernicious vomiting and inanition. The following case illustrates the therapeutic value of insulin in one of these cases.

The patient, a young married woman twenty-five years of age, developed diabetes after an acute attack of tonsillitis. Proper care was not given her until the family, realizing that she was failing rapidly, sought the aid of an eminent diabetic specialist in New York. Her tolerance was low, but on a diet of 60 gm. of carbohydrates, 60 gm. of proteins, and 145 gm. of fat—a total of 1785 calories—she was doing fairly well, excreting from 6 to 20 gm. of glucose a day, keeping her blood-sugar at a fairly constant level, a little above 200 mg. per 100 c.c., and keeping a constant weight.

Following a meal in a restaurant nausea developed followed by continuous vomiting. About three days afterward, when I saw her, the patient was in a semicomatose condition, with a feeble, irregular pulse. An attempt to evacuate the bowels with oleum ricini failed, as she vomited everything which came into the stomach, water included.

A hypodermic injection of ¼ grain of morphin gave temporary relief, but as soon as this wore off the vomiting returned. She was given 20 units of insulin intravenously that afternoon, but I was able to get only enough blood for an acetone test, which was negative. The following day, January 11, vomiting continued, and during the day she was given successive doses of insulin of 20, 10, 10, 20, and 20 units respectively. On January 12, as the vomiting had not subsided, and acetone appeared in the plasma, I gave her 250 c.c. of a 20 per cent. glucose solution intravenously, together with ¼ grain of morphin, 1/120 grain of atropin, and 40 units of insulin. A prolonged rest followed, and when the patient awoke the vomiting was practically under control. The following day she received two intravenous doses of glucose and four doses of insulin of 50, 50, 15, and 15, units, respectively, and on January 13, she received two more injections of 125 c.c. of glucose each and six doses of insulin of 25, 15, 15, 25, 15, and 15 units, respectively. After two more days on each of which an injection of 250 c.c. of glucose was given, a nearly normal status was reached. On January 15 and 16 she began to take food, and on January 17 she began to eat regular meals and to sit up in bed.

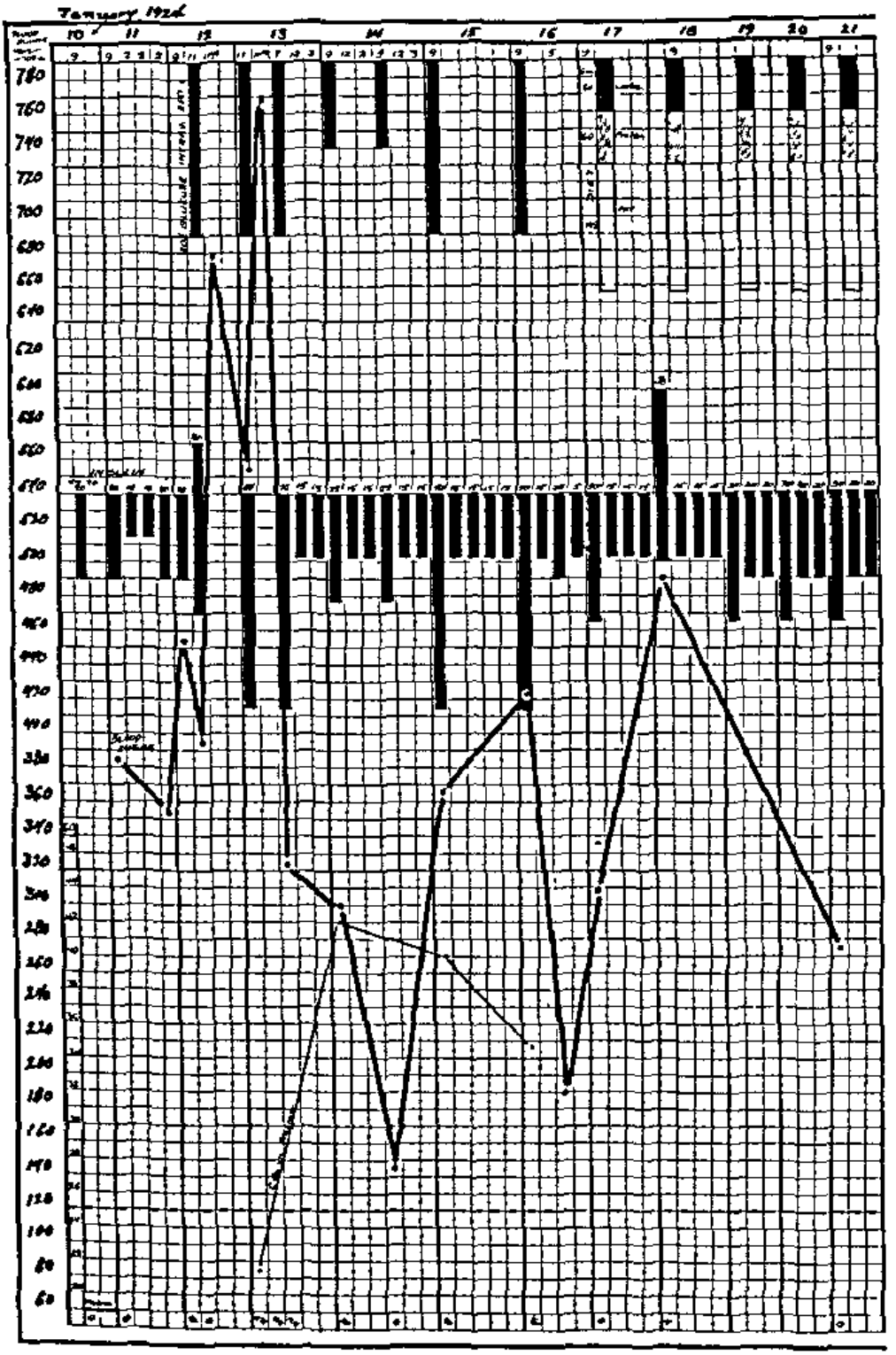

Fig. 393.—Effect of insulin on blood-sugar curve of patient with severe diabetes with acidosis and coma.

Figure 393 shows the gradually developing acidosis and coma, the low CO_2 in the plasma (21.3 at one time), and the progress under glucose (food) and insulin.

In such cases as that described above the administration of insulin must be continued until a sufficient quantity to control the condition has been given

I feel that in cases of diabetic coma with acidosis it is of prime importance to combat the inanition by giving sufficient food intravenously. Glucose is the ideal food for this treatment, since it can be given in 10 to 20 per cent solution. Insulin not only insures the proper utilization of the glucose, but it also clears up the acidosis Morphin gives rest and insures sleep

PREVENTION

The prevention of diabetes is a matter of the highest importance. Until within a few years this has been considered an impossibility, but when we consider that the marked intolerance of carbohydrates which is characteristic of the true diabetic does not occur suddenly out of a clear sky, that there is a transitory stage from the normal to the pathologic status in each case, it behooves us to discover whether or not the first stages of the process can be identified and its progress arrested

There is a border-line group of cases which we may call prediabetic, the members of which can be classified neither as diabetics nor as normal individuals, of whom we know that they will become diabetic if steps are not taken for their protection. The problem, then, is to discover which individuals belong in this prediabetic group

It is obviously impossible to test every individual to find whether or not he is a prediabetic and needs protection Fortunately, that is not necessary. But there are many individuals who bear the signs of a diabetic tendency, just as there are individuals who bear the signs of lues. In the latter case, a patient with these signs is subjected to a serologic examination to discover whether or not the assumption is correct. That is, the patient is given the benefit of the doubt. The patient who presents the signs of a diabetic tendency should be given the benefit of an examination to establish his status

Our experience leads us to consider that the following conditions may be signs of a diabetic tendency:

1. Obesity of sudden development.
2. Glycosuria.
3. A fasting twelve-hour blood-sugar of from 130 to 165 mg. per 100 c.c.
4. A blood-sugar content of 130 mg. per 100 c.c., or above three hours or more after the last preceding meal.
5. A familial history of diabetes.

I believe that the early discovery and treatment of cases presenting any of the above conditions would prevent the development of 90 per cent. of the cases of diabetes. The glucose tolerance test is the method of diagnosis. If in any case in this group the blood-sugar content returns to normal within two and a half hours after the ingestion of 100 gm. of glucose, then the normal status of the individual is established; but if it takes more than three hours for the blood-sugar to return to a normal level, then the case is potentially or actually diabetic according to the character of the curve. The glucose tolerance test, therefore, defines the line of separation between the normal and the potentially diabetic patient.

It is the patient whose blood-sugar returns to normal in about two hours and forty-five minutes who presents the opportunity for preventive treatment. Such an individual under proper instruction may remain a prediabetic with a minimum expenditure of care and a maximum efficiency for a normal length of life. The task is comparatively easy for the patient and the physician alike. In an individual in whom the pancreas is weakened, but not broken down, it is necessary only to lighten the burden of the weakened organ. This is easily accomplished by eliminating sugar and pastry from the diet and not exceeding a moderate use of bread and potatoes. It is not necessary to cut down the number of calories—the elimination of an excess of carbohydrates is sufficient. A determination of the fasting blood-sugar content once in every three months is a sufficient check on the condition.

When we consider that there are about 2,000,000 diabetics in this country today, it follows that if preventive measures are only 50 per cent. efficient—and they can be made much more

so—it will mean the saving of 1,000,000 individuals from diabetes.

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R. M. WATKINS

DEPARTMENT OF INTERNAL MEDICINE

THE PRACTICAL APPLICATION OF PROTEIN SENSITIZATION

THE determination of protein sensitivity and the use of protein therapy are proving to be valuable aids in the diagnosis and treatment of certain groups of cases. The following case reports illustrate some of the work in this field which has been in progress at the Cleveland Clinic. Thus far we have not considered the somewhat obscure relation of such diseases as migraine, epilepsy, etc., to protein sensitization, nor have we had any opportunity to study the relation of protein sensitization to the spasmodic vomiting of infancy; but all such conditions as bronchial asthma, hay-fever, urticaria, angioneurotic edema, hyperesthetic rhinitis, as well as various skin conditions, are investigated for evidence of specific protein causation.

Bronchial Asthma.—Protein tests form a part of our routine examination of all cases of bronchial asthma, but thus far a protein cause has been demonstrated in approximately only 50 per cent. Bronchial asthma may be secondary to infection elsewhere, and in a small number of cases an unsuspected pulmonary tuberculosis has been found. In the latter cases the history is often misleading, and the diagnosis is based on positive *x*-ray films of the chest and on the presence of tubercle bacilli in the sputum. These cases of asthma and tuberculosis may be sensitive also to food and to epidermal and bacterial proteins and to pollens. Cases in which the asthma is secondary to a bacterial infection are the most difficult to diagnose, but if the specific bacterial protein is found, treatment with the specific vaccine plus the usual measures of rest, diet, and expectorant mixtures will usually bring results. In patients under forty

years of age complete or very considerable relief may be expected in cases of bronchial asthma due to protein sensitivity, but in patients over forty years of age the outlook is not always so bright

Case I.—A Jewish woman thirty years of age for twelve years had had attacks of asthma These attacks varied in severity, being most severe in the fall and winter, and were often accompanied by colds When the patient came to the Clinic in January, 1923 she was suffering from a particularly bad attack, with dyspnea at night Examination revealed typical musical râles, both inspiratory and expiratory, over the whole lung area The important laboratory findings were as follows White blood-cells, 14,700, eosinophils, 7 5 per cent , blood Wassermann negative The x-ray plates of the chest and the nose and throat examination were negative Skin tests revealed marked sensitization to tomato, bean, wheat, oat, orris root, and moderate sensitivity to celery, pea, and peanut The patient was advised to eliminate the above foods from her diet and to discontinue the use of substances containing orris root, such as face powder, rouge, shampoo powders and liquids, highly scented soaps, etc Three months later she reported considerable improvement

Case II—A baby girl, two and a half years old, had developed a milk urticaria when she was weaned at four months of age, and also at about this same time, a chronic eczema For several months before coming to the Clinic she had been having severe attacks of asthma, especially after the ingestion of raw milk and eggs She was able to take condensed milk, but not plain cow's milk Examination revealed evidences of chronic eczema, the chest was quiet, as she was not having any difficulty at the time of the examination Laboratory findings were as follows White blood-count, 8000, eosinophils, 7 5 per cent The x-rays of the chest were unsatisfactory, as the patient moved Skin tests showed a marked sensitization to egg white, egg yolk, peas, wool, and dog hair No reaction to milk was obtained The mother was advised to keep the child away from her dog and to avoid wool as much as possible, the milk and egg problem was handled by giving at first very small quantities and gradually increasing them In a little over two months the child was able to take a quart of milk a day, and the sensitivity to eggs was lessening

Case III—A four-year-old boy had had infantile eczema between the ages of three months and two years For the past two and a half years during the winter he had had many attacks of asthma, with an unusually severe cough These attacks seemed to occur whenever he caught cold The physical examination showed a small, simple goiter, and a few enlarged glands, no lung signs were present, as the asthma was quiescent at the time of the examination The skin tests gave a positive reaction to the non-hemolytic streptococcus A course of injections of a mixed stock vaccine enabled the patient to go through the winter without an attack of asthma

Hay-fever.—The protein factor in hay-fever has been recognized for many years. Hay-fever appears at different seasons, and each season offers its particular cause. The common autumnal hay-fever is caused by the pollens of ragweed; the summer hay-fever is caused by the pollen of timothy. Often the pollens of other plants play a part, and there are also various abortive types. In the great majority of cases treatment brings relief, but complete non-appearance of the symptoms is unusual. None of our cases have had complete relief, but in most cases the treatment has enabled the patient to remain at work and has prevented the necessity for the enforced vacations to which these patients have been accustomed. By giving one or two maximum doses before the season begins with repeated maximum doses at intervals of a week or ten days during the early weeks of the season in which the individual case is affected, we are able to keep these patients practically immune.

Case IV.—A man, twenty-six years of age, for many years had had annual attacks of hay-fever which began in the middle of August and lasted until the first hard frost He had had serum treatment for ten seasons, and as a result had been fairly comfortable and able to keep at work. The nose and throat examination showed a slight right otitis media and a deflected septum. Skin tests showed very marked reaction to both short and tall ragweed. A course of treatment with standard solution of ragweed pollen extract, maximum doses being given twice a week for a period extending from the middle of August to September 7, resulted in practically complete relief

Case V.—A woman forty-one years of age had had rose cold for five seasons, beginning the latter part of May of each year and lasting into August. Skin tests showed a very marked timothy reaction. Treatment with timothy pollen twice a week, beginning March 15, gave almost complete relief

Case VI.—A woman twenty-six years old had had rose cold for fifteen years. It always appeared on Memorial Day and lasted into July Skin tests showed marked reactions to dahlia, daisy, rose, and timothy Desensitization with timothy pollen and avoidance of other flowers during the season gave almost complete relief.

Hay-fever and Asthma.—A report of one of our cases of combined hay-fever and asthma, in which the asthma was not due to the hay-fever, is given below:

Case VII.—A man thirty-seven years of age had had asthma for ten years, with increasing severity during the past five or six years. The asthma was present throughout the year, but was most severe in the winter The patient had also had hay-fever of the autumnal type for many years Examination of the chest revealed the usual asthmatic râles *x*-Ray plates of the sinuses showed a pathologic condition in the right antrum, the ethmoids, and the sphenoids, although lavage of the antrum returned clear *x*-Ray plates of the chest were negative Laboratory findings were as follows: Urine, very slight trace of albumin with a few hyaline casts, white blood-count, 11,600, eosinophils, 4 5 per cent Skin tests showed sensitization to lima bean, cauliflower, onion, tomato, peanut, egg-albumin, alfalfa, and ragweed The patient was desensitized to ragweed and advised to discontinue the above foods The result was practical immunity to the hay-fever and great improvement in the asthma in spite of the pathologic nose and throat findings

Urticaria and Angioneurotic Edema.—The apparent relationship between these two conditions may lie in the fact that they represent acute and chronic types of reaction to proteins It is very difficult to find the cause in many of these cases, but once found, it is usually easily eliminated The fact that these patients often exhibit a marked dermatographia, however, makes the proper interpretation of the skin reaction to proteins difficult.

Case VIII —A man thirty-four years of age gave a history of frequent attacks of hives during the strawberry season He also stated that during the past two years he had had two attacks of faintness, palpitation, tachycardia, and a considerable swelling of the face, with general malaise Each of these attacks followed the ingestion of nuts For nine years he had had also both summer and autumnal attacks of hay-fever Skin tests showed a marked sensitization to peanut, English walnut, almond, pork, timothy, and ragweed Hay-fever treatment was advised and the elimination of the objectionable foods from his diet He did not take the pollen desensitization treatment, but dietary control has kept him free from attacks of angioneurotic edema for over a year

Hyperesthetic Rhinitis (Perennial Hay-fever).—This disease is more uncomfortable than serious In most cases the cause is easily found, and good results are usually obtained These patients have violent and frequent attacks of sneezing, with a thin serous nasal discharge part or all of the time The nose and throat examinations usually do not demonstrate a sufficient cause for the trouble, but when an infection is present

it should be remedied at the first opportunity. These patients are often sensitive to more than one epidermal protein

Case IX.—A waitress twenty-one years of age complained that for two years she had had a chronic cold in the head, with frequent sneezing, coryza, and lacrimation. Nose and throat examination showed a deflected septum. The *x*-ray plates of the sinuses and the blood Wassermann were negative. Skin tests showed a marked reaction to orris root. The elimination of face and tooth powders containing orris root produced excellent results

Case X.—A settlement worker twenty-one years of age for nine months had had symptoms similar to those cited in Case IX She had a small simple goiter. The nose and throat findings were negative. Skin tests showed a mild reaction to chicken feathers and to the Bacillus pseudodiphtheriæ. Slight improvement followed the abandonment of the use of feather pillows Vaccines are now being used with some success.

Case XI.—A housewife twenty-one years of age had had a chronic cold with frequent sneezing for a year. Routine nose and throat examination was negative, but the *x*-ray plates revealed a pathologic condition in nearly all of the sinuses. Skin tests showed a mild reaction to goose feathers When this was reported, she remembered that as a little girl she was unable to work in her father's store where feathers were kept, even entering the store made her sneeze violently. The sinuses were treated and she was advised to give up the use of feather pillows, but unfortunately we have been unable to follow up the case

Dermatoses.—Recently numerous skin diseases have been found to be of protein origin, and reports of investigations along this line are appearing in the literature. We have found it very difficult, and in a large number of cases impossible, to determine the specific protein cause in this group of cases.

Case XII.—A salesman twenty-one years of age had had eczema in *infancy*, with recurrences at the ages of twelve, fourteen, and sixteen, the last attack persisting to the present time. He had suffered a great deal from itching, especially at night. The dermatological department of this Clinic diagnosed his case as one of chronic sensitization eczema. Laboratory findings showed the urine to be normal, blood Wassermann negative; white blood-count, 7600; polymorphonuclear leukocytes, 53 per cent ; eosinophils, 17½ per cent.; small lymphocytes, 26 5 per cent.; transitionals, 2½ per cent.; basophils, 0 5 per cent ; blood chemistry normal, basal metabolism, —8. Skin tests showed a marked sensitization to ragweed, timothy, chicken feathers, goose feathers, horse dander, and tobacco; a moderate reaction to strawberry, oat, wheat, and sunflower, and mild reaction to squash and onion The patient was advised not to use feather pillows and to avoid tobacco and the foods

mentioned above Such marked improvement followed this treatment that no pollen desensitization treatment was given. In seven months the skin of the patient was practically clear He still has to use care, however, as a session of card playing in a room thick with tobacco smoke, for example, will bring on a recurrence of the symptoms

Case XIII.—A Jewish woman fifty-six years of age had arterial hypertension and what was thought to be scabies. Treatment for the latter condition did not relieve the itching Skin tests showed a positive reaction to colon bacillus Vaccine treatment with colon bacillus cultured from the patient's stool resulted in relief

DISCUSSION

In connection with this brief summary of case reports a short description of our methods of protein sensitization may be of interest

We have found the cutaneous scratch method, advocated by Walker, very satisfactory Five parallel scratches from 2 to 3 cm apart and about 1 cm long are made with a sharp-pointed knife The site chosen for the test is usually the surface of the upper arm where there is the least amount of hair, though when many tests are made the need for more space sometimes makes it necessary to extend the rows to the flexor surface of the forearm Occasionally surfaces on the lower leg or on the back are used In some cases, particularly in small children, three parallel scratches may be sufficient. If the protein is in solution or in the form of paste, it is applied directly to the scratch, if in a powder, a drop of one-tenth normal sodium hydroxid solution is placed on the scratch before the powder is added so that the powder may be dissolved in the hydroxid

Reactions are determined by the presence or absence of an urticarial wheal, at first pale, surrounded by a zone of redness which forms within half an hour after the application of the proteins except in the cases of bacterial proteins, when the reaction may be delayed for from twenty-four to forty-eight hours We have adopted the index used by several workers, namely, that the wheal must be of the typical urticarial type, giving off pseudopodia, and at least 0 5 cm. in width In normal individuals a scratch will often cause an elevation of the skin, but wheals will not develop unless the skin be dermatographic

Sensitivity to the pollens of ragweed and timothy may be overcome during the pollinating season by the injection of properly graduated doses of their protein extracts. Other causative pollens can be avoided easily, since they do not travel far in ordinary weather. Food sensitivity can be combated either by avoiding the offending foods or by desensitization produced either by the injection of food protein extracts, or by the ingestion, with the meals, of infinitesimal quantities of the specific food, the amount of which is gradually increased until a satisfactory quantity may be eaten with impunity. The epidermal proteins are usually easily avoided, but desensitization may be produced by means of the proper protein extract. Bacterial desensitization may be accomplished by vaccines, provided the foci of infection be cleared up and general treatment instituted to build up the resistance, etc.

The number of different proteins to which one patient may be sensitive is very important. A clue may be obtained from the clinical history, but cutaneous tests with a large number of proteins will not only confirm the diagnosis but also often bring to light other unsuspected causes. For example, the patient whose case has already been cited (Case VII) was suffering from both hay-fever and asthma, each of which was due to a different type of protein—one to pollen and one to food.

Among 184 cases of diseases due to protein sensitivity, positive reactions have been obtained in 101, or 55 per cent., and among these 101 cases the reactions were multiple in 60 per cent.

EARL W. NETHERTON

DEPARTMENT OF DERMATOLOGY

HERPES ZOSTER ASSOCIATED WITH PARALYSIS

ALTHOUGH several cases of muscular paralysis accompanying or following an attack of herpes zoster have been reported, the occurrence of this complication is so uncommon that additional reports are warranted. Recently 2 cases of herpes zoster with involvement of the regional motor nerves have been observed, one a case of herpes occipitocollaris, with facial paralysis, and the other a case of repeated recurrence with only partial paralysis or impaired function within the affected zone.

Fig 394.—Herpes zoster involving second, third, and fourth cervical nerves, with paralysis of seventh nerve on right side

Case I.—The patient, an accountant twenty-seven years of age, came to the Cleveland Clinic March 30, 1923, complaining of paralysis of the right side of his face (Fig. 394). With the exception of diphtheria at the age of six

About March 1st he had noticed a pain in
...elling of the right
cervical glands ... of air while
working. Within two days a typical eruption ... developed, which involved the right side of the neck and extended down the chest, anteriorly, to slightly below the level of the third rib, and posteriorly, to the midline and up into the scalp. A few vesicles were observed as low as the sixth cervical spine. There were a few lesions near the right angle of the mandible and also in front of the ear. The auricle, auditory canal, and tympanic membrane were free from lesions. Two weeks after the appearance of the eruption the paralysis appeared. The hearing was not affected. The sense of taste was diminished on the anterior part of the right half of the tongue, which was sensitive to a pin prick, and the patient complained of a feeling of smoothness on this area. There were no lesions on the mucosa and deglutition was not impaired.

The general physical examination was negative except for a total right-sided facial paralysis and an elevated blood-pressure of 174/100. The pulse-rate was 72 per minute and the temperature 98.2° F. Subjective symptoms of severe burning and tingling over the affected area were present. The muscles of the right side of the face reacted well to galvanization, but only slightly to faradization. The laboratory findings were as follows:

Urine.—Reaction, acid, specific gravity, 1014; albumin negative, sugar negative, microscopic examination negative.

Blood.—Red blood-cells, 5,180,000, white blood-cells, 12,500, hemoglobin, 85 per cent. (Dare). Differential count: polymorphonuclear neutrophils, 60 per cent., eosinophils, 0.5 per cent., small lymphocytes, 38.5 per cent., Wassermann negative.

Case II.—A battery salesman, twenty-eight years of age, came to the Cleveland Clinic on July 9, 1923, complaining that he had had recurrent attacks during the last thirteen years of a painful vesicular eruption involving the right side of the forehead (Fig. 395). The attacks had occurred regularly once a year and always between the 1st and 10th of July. The eruption first appeared during his freshman year in college. The number of different places in which he had lived since that time and the variety of his occupations ruled out any possible environmental or occupational factor as a contributing cause. The eruption was always preceded by prodromal symptoms of burning and itching of the skin over the right eye near the supra-orbital notch. There was also some pain in this region. Within two or three days a vesicular eruption would appear. Recovery was usually complete in from ten days to two weeks. The patient had become so accustomed to these attacks that he had ceased to consult a physician, but the severity of this last attack alarmed him to such an extent that he came to the Clinic. The extent of the eruption was about the same as usual, but the pain was more severe and the area involved included the right half of the scalp and upper part of the right arm. His scalp was so sensitive the first two days of his illness that he was unable to wear a hat. His right arm ached and he had difficulty in closing his hand.

The general health of the patient had always been good. Except for

scarlet fever in 1900 he had never had a serious illness He smoked eight cigarettes a day; otherwise his habits were good. When he came to the Clinic for consultation the pupils were equally regular and reacted to light and accommodation; the mouth and throat were negative; the teeth were negative except for an abscessed lower left first molar

On the right side of the forehead, extending from the eyebrow upward to the hairline, the skin was swollen and red and presented numerous groups of small vesicles Most of the vesicles had undergone some involution, with some crusting. There was slight ptosis of the right upper eyelid. The skin in front of the right ear was swollen and the lymph-glands in this region were tender Tenderness was also present over the right mastoid process and

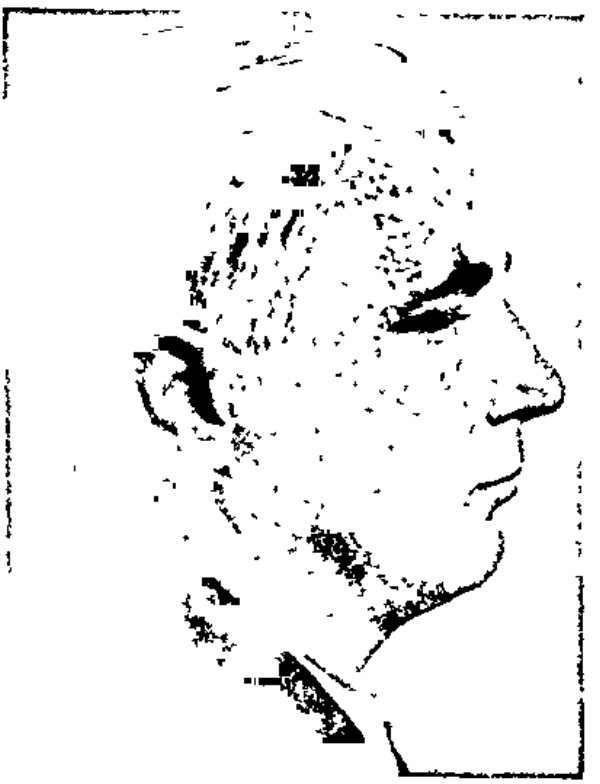

Fig 395.—Herpes frontalis, with impairment of muscular action of right side of face

over the right side of the scalp The auditory canal, auricle, and tympanic membrane did not present vesicles, and there was no evidence of middle-ear disease. Although there was no facial paralysis, a definite impairment of muscular action on the right side of the face could be demonstrated. Hearing and taste were not disturbed.

The patient was given symptomatic treatment and the abscessed tooth was extracted He did not return for further observation.

It is not the purpose of this communication to discuss in detail the subject of herpes zoster, but rather to consider a few

facts relative to the occurrence of paralysis as one of its complications. However, a brief statement as to the nature of herpes zoster may be given.

Herpes zoster is an acute, specific infectious disease of the nervous system, characterized by a vesicular eruption and pain in the course of one or several sensory nerve-roots. Usually, the ganglia of one side only are attacked, and the pain and eruption are limited to the skin zone governed by the affected ganglia The lymph-glands become swollen and there may be an elevation of temperature, leukocytosis, and general exhaustion Pain and paresthesia in the affected zone may last several days after the eruption has disappeared Owing to the specific nature of the affection recurrent attacks are rare The pathology consists of an acute hemorrhagic inflammation of the posterior root ganglion, with more or less extension to the efferent and afferent nerve-fibers. This is followed by sclerotic and degenerative changes depending upon the severity of the acute inflammatory reaction.

The exact nature of the infectious agent is not known Montgomery[5] believes, as was originally reported by Rosenow and Oftedal, that it is probably of streptococcus origin, the infection reaching the ganglion from the skin by way of the peripheral nerves or perineural lymphatics In a recent preliminary report of experimental work with herpes virus Teague and Goodpasture[10] state that they have concluded that the virus first multiplies at the site of inoculation in the skin and reaches the spinal ganglion by way of the corresponding spinal nerve These investigators found that skin which had been irritated with tar to the point of epithelial proliferation was apparently more susceptible to the virus than normal skin They cited the work of Lipschutz and that of Levaditi, in which they were able to produce herpetic eruption by the inoculation of herpes virus obtained from herpetic lesions Stern,[9] however, considers idiopathic herpes zoster as a general infectious disease which may or may not be accompanied by the herpetic eruption

Herpes zoster is a comparatively common disease, comprising about 1 5 per cent of the cases of skin disease. Approxi-

mately 76 per cent. of the cases involve the trunk (Hewlett, quoted by Montgomery), although paralysis is most frequently seen in herpes of the cephalic extremity. Hunt[2] collected 158 reports of cases in which herpes zoster was accompanied by paralysis. In 140 cases the cephalic extremity was involved, and in 18, the trunk.

Doucet (quoted by Neve[7]) collected 26 cases of herpes associated with facial paralysis, the eruption appearing in the following places: face, 27 per cent.; neck, 19 per cent.; auricle, 4 per cent.; tongue and palate, 19 per cent.; face and neck, 19 per cent.; face, neck, and mouth, 4 per cent. In 4 cases out of 26 the hearing was affected.

Worster-Drough[12] recently reported a case of herpes zoster affecting the twelfth thoracic nerve, followed by paralysis of the muscles in the lower part of the abdominal wall of the same side. He cites a case reported by Soderbergh in which the herpes involved the fifth and sixth thoracic segments with slight paralysis of the external oblique muscle on the same side.

Bloedorn and Roberts[1] observed a paralysis of the posterior portions of the abdominal muscles in a case of herpes zoster in which the eleventh left thoracic nerve was affected. On standing or when the intra-abdominal pressure was increased a marked protrusion was noticed in the left lumbar region, the muscles in this region being flaccid.

In a case observed by Weber[11] the herpetic eruption involved the left side of the head and neck, the left clavicular region, shoulder, and upper left chest. The eruption was preceded for a period of seven days by sudden paralysis of the left arm. There was also an ankle-clonus on the left side, with a suggestive Babinski. Weber gives a brief outline from the literature of 11 cases of brachial herpes associated with complete or partial paralysis of the arm, and includes also an excellent list of references with abstracts of several previously reported cases

The 2 cases reported above belong to a syndrome originally described by Hunt[4] and later discussed by Sharpe.[8] Hunt showed that the geniculate ganglion (sensory ganglion of the facial nerve) and the peripheral ganglia of the acoustic, glossopharyn-

geal, and vagus nerves may also be the seat of herpetic inflammation He also outlined a zoster zone for each ganglion. These ganglia, like the spinal ganglia and the ganglion of Gasser, are developed from outgrowths of the neural ridge, and with the exception of the ganglion of the acoustic nerve are of the unipolar or spinal cell type. This histologic and embryonic similarity places them within the realm of herpes zoster The ganglion acousticum, which becomes differentiated into the spiral and scarpa ganglia, retains its bipolar type of cell. This, however, does not remove it from the realm of zoster, as is shown by the occurrence of auditory symptoms in herpes of the face, neck, and ear. These may vary from a slight disturbance in hearing to severe tinnitus aurium, deafness, vertigo, vomiting, nystagmus, *and disturbance of equilibrium—Ménière's syndrome.*

Hunt emphasizes the fact that the inflammatory reaction may occur in ganglia above or below the chief focus or ganglion giving rise to the eruption He regards the gasserian ganglion, the geniculate, the peripheral ganglia of the acoustic, glossopharyngeal and vagus nerves, and the second, third, and fourth cervical ganglia as representing a ganglionic series or chain in which one or more ganglia may be involved in a herpetic inflammation, producing a definite symptom complex or syndrome

In order to understand this syndrome it is important that certain anatomic facts be known (Fig. 396). The facial nerve is a mixed nerve, having as its sensory portion the geniculate ganglion, the superficial petrosal nerves and the chorda tympani being the afferent sensory fibers, and the portio intermedia, the efferent fibers The facial and acoustic nerves, with the portio intermedia lying between them, enter the internal auditory meatus Within the meatus the nervus intermedius sends communicating branches to each nerve All three nerves lie close together and are surrounded by a common sheath The geniculate ganglion is an oval swelling on the facial nerve It is located in the canalis facialis at the point where the facial nerve bends backward and receives fibers from the upper or vestibular trunk of the acoustic nerve From the geniculate

ganglion three small nerves arise: (1) the greater superficial petrosal nerve, which passes forward through the hiatus canalis facialis and, after being joined by the deep petrosal nerve, ends in the sphenopalatine ganglion; (2) the ramus anastomoticus cum plexu tympanico, a small nerve which pierces the temporal bone and joins the tympanic branch of the glossopharyngeal, forming the lesser superficial petrosal nerve, which, after piercing the temporal bone, ends in the otic ganglion; and (3) the external superficial petrosal nerve, a minute inconstant branch

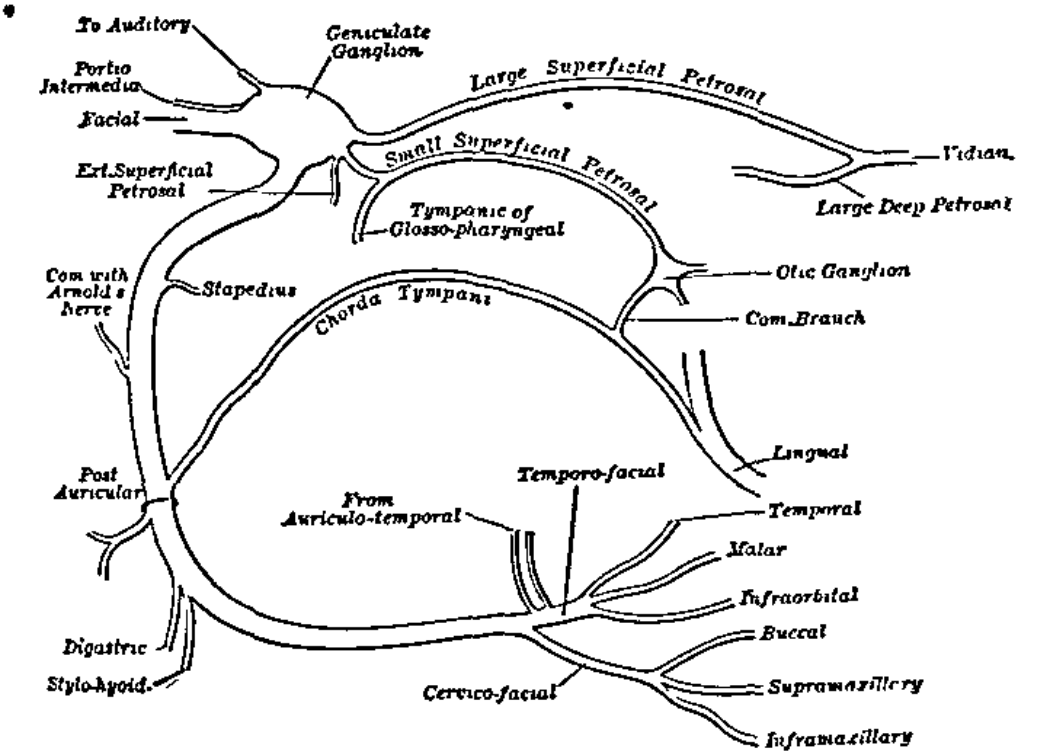

Fig 396.—Plan of the facial nerve. (From Gray's Anatomy, 1905 Edition, Fig. 677.)

which joins the sympathetic plexus on the middle meningeal artery. Three nerves arise from the facial nerve before it emerges at the stylomastoid foramen: (1) the stapedius nerve, which supplies the stapedius muscle; (2) the chorda tympani, which enters the tympanic cavity through the tympanic aperture of the canaliculus chordæ and reaches the infratemporal fossa by passing through the medial end of the petrotympanic fissure, joining the lingual branch of the mandibular nerve beneath the external pterygoid muscle; this nerve supplies a root to the

submaxillary ganglion and finally is distributed to the side and dorsum of the tongue in its anterior two-thirds; and (3) a communicating branch which joins the auricular branch of the vagus nerve.

Hunt's syndrome may be divided into the following clinical types.

1. **Herpes Oticus.**—This is the simplest type of the syndrome The geniculate ganglion is the site of the herpetic inflammation, and the resultant vesicular eruption appears in a cone-shaped area composed of the posterior half of the tympanic membrane, external auditory canal, the concha, the antihelix and its fossa, the antitragus, and a portion of the lobule (Sharpe[8]). Preherpetic pains may localize in the ear and mastoid, causing one to suspect that the patient is suffering from a mastoid infection Postherpetic otalgia may be persistent.

2 **Herpes Oticus with Facial Paralysis.**—The adjacent facial nerve is involved in the inflammatory process, with resultant paralysis The paralysis is complete, and may vary from a transient form to permanent weakness or paralysis.

3 **Herpes Oticus with Facial Paralysis and Acoustic Symptoms.**—Associated with the paralysis due to the extension of the inflammatory process from the geniculate ganglion to the facial nerve auditory symptoms may occur. These may vary from a hypo-acousis to the severe cases in which there is tinnitus aurium, deafness, vertigo, nystagmus, nausea, and vomiting. These symptoms are produced by the involvement of the auditory nerve within the auditory canal or to a simultaneous inflammation of the auditory ganglia

4 **Herpes Occipitocollaris with Facial Paralysis.**—In this type of zoster the chief focus of inflammation is in the second, third, and fourth cervical ganglia, with eruption on the neck and occipital region There is also involvement of the geniculate ganglion, with or without the eruption in the geniculate zone Some cases present auditory symptoms In cases of herpes zoster facialis in which the chief focus is the gasserian ganglion there may be simultaneous involvement of the geniculate ganglion, with facial paralysis

The frequent occurrence of paralysis in cases of herpes zoster of the cephalic extremity may be explained by the close relationship of the ganglia of the seventh, eighth, ninth, and tenth cranial nerves to the corresponding nerve-fibers. These ganglia, unlike the gasserian and spinal ganglia, have no fibrous capsule which could in a measure protect the motor nerve-fibers from the extension of the herpetic inflammation. Montgomery[6] is of the opinion that the rôle of immunity rather than the anatomic relationship determines the location of paralysis in cases of herpes zoster. He believes that the virus reaches the ganglion by way of the skin and perineural lymphatics, and that in herpes zoster of the trunk and extremities, during the passage of the virus along the peripheral nerves, a sufficient immunity has been established to protect the motor fibers. This explanation seems hardly sufficient As in other infectious diseases, the severity of the attack is governed by the resistance or susceptibility of the patient and the virulence of the virus However, the close relationship of the ganglia of the cranial nerves and their corresponding motor fibers and the absence of a fibrous capsule is sufficient to explain the comparatively frequent occurrence of the extension of the herpetic inflammation to the closely placed motor fibers, with resultant paralysis in herpes zoster of the cephalic extremity. The immunity reaction and the anatomic relationship combined probably determine the occurrence of paralysis as a complication of zoster.

Weber,[11] Neve,[7] and Stern[9] are of the opinion that paralysis of isolated muscles or groups of muscles, idiopathic facial paralysis, and unexplained unilateral mydriasis may be manifestations of an attack of herpes zoster without any herpetiform eruption.

In the first case reported the fact that the facial paralysis was of the lower neuron type, with no eruption in the geniculate zone, demonstrates that in a herpetic eruption there may be an involvement of the geniculate ganglion with an associated facial paralysis without the occurrence of an eruption within the zone of that ganglion. Therefore, Neve's question seems to be pertinent: "Why should not facial paralysis be the sole symptom of

an inflammation of the geniculate ganglion caused by the same virus which produces typical herpes zoster elsewhere?"

The most interesting feature of the second case reported is the history of repeated attacks of herpes zoster occurring at the same time each year and always involving the ophthalmic branch of the fifth cranial nerve For this periodicity I have no explanation to offer The regular periods of freedom from attacks might be explained as due to a temporary immunity, but the occurrence of the attacks at exactly the same time each year cannot be accounted for in this way. Each attack was preceded by the characteristic prodromal symptoms of zoster, and the patient was confident that each attack had been similar to that described above Therefore the conclusion that each attack was, in reality, one of zona seems warranted. There was definite evidence of partial paralysis of the facial nerve of the affected side, and pain in the arm gave evidence of involvement of the cervical ganglia

CONCLUSIONS

1 Two cases of herpes zoster of the cephalic extremity with paralysis are reported, each belonging to the syndrome first described by Hunt.

2 That the geniculate ganglion, the ganglia of the eighth, ninth, and tenth cranial nerves, and of the second and third cervical spinal nerves are a ganglionic chain or series, in which one or several may be simultaneously involved in a herpetic inflammation, is demonstrated by each case

3. No explanation for the periodicity of zona in the second case can be given

4 That "idiopathic" facial paralysis may be a manifestation of an attack of herpes zoster without any herpetic eruption seems plausible.

5 The tenderness over the mastoid process in the second case demonstrates the importance of establishing a differential diagnosis between herpes zoster and mastoiditis in any case in which the presence of either is suspected, but not clearly defined

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DEPARTMENT OF ORTHOPEDICS

PERIARTHRITIS OF THE SHOULDER

With Special Emphasis on the Value of Diathermia in Its Treatment

THE term "periarthritis of the shoulder" is here used to describe a type of disability which is designated by various terms, such as "subacute neuritis," "subdeltoid bursitis," "sprained shoulder." Physicians have dreaded to encounter these patients who come in complaining of "painful shoulder," because it has been difficult to arrive at an accurate diagnosis as to the exact condition; to determine the best method of treatment; and especially to maintain the persistence and general morale of the patient throughout the usually protracted term of treatment.

That there is as yet no unified opinion among orthopedic surgeons as to the best procedure to follow in these cases is illustrated by Case I which is cited below. This patient had consulted two surgeons of the highest standing in New York, one of whom recommended removal of the calcified area; the other manipulation. She found the same difference of opinion in Boston, where one orthopedist recommended open operation for removal of the calcification and another manipulation.

The frequent occurrence of this condition—we have seen 47 cases in the last eighteen months—and the good results which we have secured by the addition of diathermia to the other generally accepted methods of treatment has suggested this discussion.

The following case presents a classical picture of chronic subdeltoid bursitis or periarthritis of the shoulder:

allel to bone.

Fig. 397 —Calcified area in

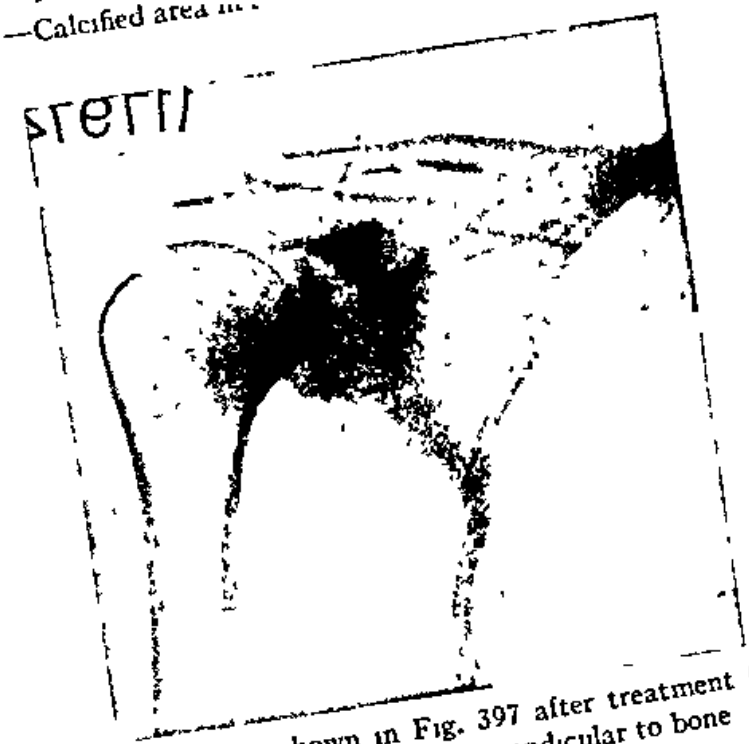

Fig. 398 —Calcified area shown in Fig. 397 after treatment for fifty days, partially absorbed and perpendicular to bone

Case I.—Two years before we saw her this patient had strained her right upper arm while playing golf, and ever since she had experienced varying degrees of discomfort in the right arm and shoulder There was limita-

tion of abduction and internal and external rotation, but the anteroposterior movement of the shoulder was quite free. An *x*-ray examination showed a calcified mass lying close to the head of the right humerus (Fig. 397). The patient was sent into the hospital, where under anesthesia the adhesions were broken down by manipulation, after which the arm was flexed and extended above the head. The arm was kept in this position, excepting for periods of treatment for three days, when the patient was discharged from the hospital wearing a Jones abduction splint, but continued to come to the Clinic daily for passive and gradually increasing active exercises and diathermia.

Fig. 399.—Complete disappearance of calcified area shown in Figs. 397 and 398. Roentgenogram taken six months after that shown in Fig 398.

Eighteen days after the manipulation free movements of the shoulder could be obtained and there was no pain on pressure over the subdeltoid bursa, but voluntary movements still caused some discomfort.

Fifty days after the manipulation an *x*-ray examination showed that the calcified area seen in Fig. 398 had been displaced downward and outward so that its position was approximately at a right angle to the head of the humerus, and there was considerable absorption of the calcified area (Fig. 398). At this time the patient was given advice regarding exercises which she could carry out at home.

Six months later she reported at the Clinic. At that time she had practically no pain in the shoulder and could move her arm in every direction.

There was a very slight limitation of internal rotation, but she could reach the small of her back without pain An *x*-ray plate taken at this time showed that the calcified area had been completely absorbed (Fig 399)

The following case is of interest because of the development of a very acute periarthritis of the shoulder as the result of trauma in a case of chronic subacute bursitis of long standing, all symptoms disappearing completely and apparently permanently after treatment:

Case II.—For some years—at least five—the patient had had recurrent attacks of boring pain in the outer aspect of the upper third of the right upper arm I first saw her four days after she had shaken hands at a reception with over 1000 people At that time there was definite limitation of motion and tenderness on pressure along the outline of the subdeltoid bursa, with considerable ecchymosis. *x*-Ray examinations of the teeth and sinuses for possible foci of infection were negative An *x*-ray plate of the right shoulder showed a roughening over the acromion near the clavicular union, directly beneath the site of the swelling of the soft parts

Diathermia, light massage, and abduction were prescribed, and definite improvement was in progress when the patient slipped on an icy sidewalk *and fell, striking her shoulder against a hydrant* The intense pain, very extensive ecchymoses, and almost complete limitation of motion made it necessary for her to enter the hospital, where her arm was kept extended above her head except for daily periods of passive movements and light massage After twelve days in the hospital the arm was put up in a Jones abduction splint and daily diathermia treatments and exercises were given The splint was worn for about three weeks, but the diathermia and exercises were continued for two weeks longer.

At the end of this time, forty-four days after the acute injury, all pain had disappeared and the arm functioned freely with full internal and external rotation and full abduction One or two brief periods of subsequent discomfort were promptly controlled by diathermia Up to the present time, seventeen months after the final treatment, there has been no return of any symptom

As is illustrated by the above case reports, after severe or mild injuries or shocks to the shoulder, there often develops an extremely painful condition which involves the whole arm suggesting the diagnosis of neuritis, although true symptoms of neuritis are absent, for there is no tenderness over the brachial plexus or its constituent nerves, no swelling of the hand, and no disturbance of sensation The arm feels heavy and the wearing of a heavy coat or carrying a bag gives rise to great pain. As a

result the arm too often is habitually carried at the side and is not moved unnecessarily.

The most common designation of this condition is "subdeltoid bursitis." From my personal observations I am inclined to believe that when there is any affection of the bursa this is generally associated with other changes about the joint. It is often impossible to differentiate between the movement of the deep bursa and of the capsule of the joint. It is for this reason that it seems to me better from the therapeutic point of view to regard the condition as one which involves the joint structure as a whole, and to include all types of the condition under the one term "periarthritis of the shoulder."

Some form of traumatism is the usual cause of periarthritis of the shoulder, the most common injuries being a fall upon the shoulder or a violent twist or wrench of this articulation, such as a fall on the outstretched hand, which may have resulted also in a Colles fracture or some other injury. Thus, in one of our cases the periarthritis followed a fall forward on both hands which resulted in a fracture of the neck of the radius, with arthritic processes in the elbow and superior radio-ulnar joints. There was definite limitation of shoulder movement. This case is still under treatment, but already, six months after her fall and two months after she first came to the Clinic, there is marked improvement in the shoulder as well as in the elbow and hand as the result of manipulation, massage, and diathermia.

Anatomic Consideration.—In order to locate the site of the lesion in cases of periarthritis of the shoulder, it will be well to consider the anatomic structure of the shoulder-joint. An examination of the origin and insertion of the deltoid and supraspinatus muscles will show that the first action of the deltoid in contracting must be to press the humerus up against the acromion and then to abduct it. The supraspinatus muscle, on the other hand, has only one function—that of abduction. These two muscles are used to raise the arm from the side, and, accordingly, weakness in abduction does not necessarily indicate an affection of the deltoid only, but it may be due to some abnormal condition of the tendinous insertion of the supra-

spinatus. It is absolutely impossible for mere pressure at the examination to elicit the real site of the difficulty; that is, whether it is the bursa, the tendon attachment, or the capsule under the tendon that is affected.

Internal rotation is produced chiefly by the action of the pectoralis major and the subscapularis muscles and in small part by the teres major. The pectoralis major is accessible to palpation throughout, and the course of the broad tendinous insertion can be followed to its termination in the outer bicipital ridge of the humerus. The subscapularis tendon is in part inserted into the ligament of the shoulder-joint and in part into the tuberosity and neck of the humerus The tendon is thus in close contact with the anterior part of the capsule. A resisted attempt at internal rotation could thus result in pain, not only from the involvement of the subscapularis tendon but also from injury involving the capsule in this region

When the cause of pain on internal rotation is an injury of the pectoralis major, this may be identified by palpation of the muscle. If there is resisted internal rotation of the shoulder and the pectoralis major is not the seat of injury, then the pain is due to an affection of either the subscapularis tendon or of the anterior part of the capsule

External rotation is produced by the infraspinatus muscle aided by the teres minor. The infraspinatus muscle terminates in a tendon which glides over the internal border of the spine of the scapula, passes behind the capsular ligament of the shoulder-joint, and is inserted into the middle part of the greater tuberosity of the humerus. A synovial bursa sometimes separates the tendinous portion from the capsule of the joint This muscle is one of the important protections of the joint, guarding it from dislocation backward, but it is not one of the muscles commonly affected by muscular strain

The biceps tendon is associated with the capsule of the shoulder-joint The following movements give the best indication of injury of the tendon of the biceps muscle· With the arm at the side (1) supinate the forearm, or (2) flex the elbow against resistance If either of these movements causes pain,

then the biceps tendon is involved. Tenderness over the biceps tendon can be found by pressure in the bicipital groove of the humerus, which is identified by holding the arm at the side, with the palm facing forward, when the groove can be felt at the inner side of the acromion process passing downward on a line with the middle of the arm; if the forearm is flexed, the tendon of the biceps can be felt to move over this groove. Swelling and tenderness in this region is very suggestive of injury to the long head of the biceps.

As for the subdeltoid bursa itself, under normal conditions it is situated beneath the fibers of the deltoid muscle and directly above the fibrous capsule of the shoulder-joint, covering an area as large as the palm of the hand. As a rule, the bursa is not connected with the shoulder-joint itself, but in some instances it is. Codman[1] has demonstrated admirably the rôle played by this bursa in movements of the shoulder. Normally the bursa has very thin walls, contains a certain amount of fluid, and adapts itself accurately to the different positions of the head of the bone as they change with motion of the arm, thus allowing the free gliding movements of the bone under the muscles. When the shoulder is contused or strained the most common reaction is an increase of fluid in this bursa, just as "water on the knee" develops after an injury to that joint. If the twist is severe, the tissues may be torn (the supraspinatus tendon capsule, etc.), with a resulting hemorrhage into the sac and the capsule of the joint. Then, as this exudate organizes, the entire membrane becomes thickened with resultant partial or complete obliteration of the cavity within. Sometimes, in certain areas of the sac, villous enlargements have been seen which are so dense as to give a definite shadow on the *x*-ray plates. The débris may become organized and even calcified, thus giving the characteristic *x*-ray appearance.

Occasionally the immediate effects of injury are insignificant, the true symptoms of the periarthritis developing several days afterward as the adhesions begin to organize. Thus, an injury to the shoulder may cause very little pain at first, but after about ten days there may be excruciating pain on any move-

ment Great discomfort is experienced by these patients, especially at night It is almost impossible for them to assume a comfortable position because of the dragging back of the humerus when in the supine position or when lying on the well side If they do get to sleep, they are suddenly awakened by any movement, and lying on the affected side is usually impossible

Signs and Symptoms—The chief clinical characteristics of periarthritis are practically constantly present There is no conspicuous alteration in the contour of the shoulder, but in the chronic cases there may be more or less atrophy, especially in the deltoid and supraspinatus muscles.

There is marked impairment of function of the shoulder-joint with limitation of external and internal rotation and of abduction There is practically always free movement in the anterior posterior direction, which indicates that the shoulder-joint itself is not involved, as it is well known that *free movement of a joint in any one direction differentiates the periarthritic from the true arthritic case.*

As a rule the *x*-ray report of the shoulder is negative, but in a few cases definite calcification will be found in the subdeltoid and the subacromial bursa.

Acute localized tenderness on pressure is often demonstrable over the edge of the subdeltoid bursa or over the tendon attachments about the joint, the cause of which will have to be identified according to the anatomic relations which have been described above

Treatment—The general treatment of these cases must include a painstaking search for all possible foci of infection and the elimination of any suspicious point of origin Teeth roots, tonsils, sinuses, gastro-intestinal, and genito-urinary tracts must all be given thorough consideration, as otherwise the local treatments will be greatly prolonged and probably unsuccessful In the recent or acute case we have adopted the following plan of local treatment

The arm is held in abduction on a Jones abduction splint and ice-caps are applied in an attempt to limit the amount of hemorrhage and effusion about the joint. On the third day

sedative diathermia is given to increase the hyperemia and so produce increased absorption and aid the repair of the damaged tissues The arm is passively moved (once on'y) through the full range of abduction and of internal and external rotation, and is then fixed again in abduction The above treatment is carried out daily and as much voluntary contraction of the deltoid and other muscles is encouraged as is possible without pain.

As the range of voluntary movement without pain increases, the degree of passive abduction is gradually decreased until full active abduction is possible without discomfort. The abduction splint is then discarded and full voluntary movements are encouraged until full function is restored.

In the chronic case in which adhesions have formed and any attempt at passive movement causes severe pain and results in swinging of the scapula, a manipulation of the shoulder is considered necessary before any other treatment is undertaken. The patient is anesthetized with nitrous-oxid-oxygen and the shoulder is manipulated so as to break down the adhesions and the shoulder is then treated as an acute case. I would like to emphasize an important point in relation to the manipulation. This must be done deliberately and gently—the arm being forced through full abduction, internal and external rotation, the arm then being fixed in abduction on a splint after all adhesions have been broken. One cannot give too strong a warning against overzealousness in the manipulation, and any "pump-handle" action must be avoided. The point is to break the adhesions, and that only, as it is essential to avoid causing any more reaction about the joint than is absolutely necessary.

There are certain borderline cases with some adhesions which respond to diathermia without manipulation. In such cases the adhesions gradually soften and absorb under treatment with diathermia, passive movements, and massage One learns to differentiate between those cases which require these treatments only and those in which nothing will be effectual without manipulation.

As many are not as yet familiar with the use of diathermia,

I feel that a short explanation of its application in these cases may be of value. The effects of sedative diathermia may be summarized as follows:

1. The formation of heat in the tissues
2. The localization of heat
3. The production of active hyperemia
4. The solvent effect of fibrous adhesions
5. The absorption of traumatic débris in the subdeltoid bursa and capsule of the joint as the result of the increased phagocytosis produced by the hyperemia.

Many types of electrodes are in use, but we have found a sponge electrode on the top of the shoulder and a chain or metal cuff electrode around the upper arm to be most satisfactory. It is important that the electrodes as well as the skin should be well moistened and a lather of soap applied evenly before the electrodes are attached. A pleasant and soothing feeling of warmth is the only sensation the patient should experience during the application of a sedative diathermia treatment. The arm should be carefully supported on pillows in an abducted position in order to secure the maximum relaxation of the deltoid muscle during the treatment

Before anyone attempts to treat this type of case he must be sure that *sedative* diathermia is being given, for should the current be stepped up too quickly, with a resultant *stimulative* treatment, very disastrous results are bound to follow. The pain will be much increased and the patient will certainly look elsewhere for relief.

Before commencing a sedative diathermia treatment it is most important to make sure that the spark-gap is shut. As soon as the electrodes have been carefully applied the current is switched on and the rheostat moved up very slowly, after which the spark-gap is opened slightly. After a short period the spark-gap is closed and the rheostat again advanced and the spark-gap opened further. These procedures are continued gradually until the galvanometer registers the amount of current which is to be applied. From five to ten minutes should be taken in stepping up the current, and it is also just as important when finishing a

treatment to turn the current off slowly, as any stimulative action at the end, as at the beginning, will abort the whole result of the treatment. We have had our best results with treatments of considerable length, *i. e.*, from forty-five minutes to one hour with a low current of about 300 to 400 milliamperes.

In the acute stages of periarthritis of the shoulder very little massage should be given, as it is apt to stir up the reaction. As the acute stage subsides the current may be gradually increased and the diathermia treatment followed by gentle massage, a greater range of passive movements, and a few active exercises. As the pain subsides the active exercises should be increased to prevent the formation of adhesions.

In the older cases in which adhesions have already formed a slightly higher current is given in order that the resultant hyperemia may soften the adhesions and resolve the fibrous tissues, the diathermia treatment being followed by deep massage and passive and active movements in order to stretch the softened adhesions.

The results of treatment along the above lines have been most gratifying. The acute cases respond very rapidly and the chronic cases ultimately give most excellent results. We have seen cases in which the calcified deposits in the bursa have completely disappeared. Not so many years ago it was strongly urged that all cases with calcified deposits should be operated upon in order to dissect out the bursa, but from my own experience treatment along the above lines is the most effective line of treatment in these cases.

As stated above, in the past eighteen months we have seen 47 cases of periarthritis of the shoulder, of which 35 have been treated. Four cases showed calcified bodies and 11 required manipulation under anesthesia. Among the 35 cases treated, 27 (77 per cent.) have been cured, 6 have improved, and only 2 have shown no improvement.

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THE RÔLE OF DENTAL INFECTION IN THE PRODUCTION OF CERTAIN APPARENTLY UNRELATED CONDITIONS

THE following cases, in each of which the condition for which the patient sought relief was cleared by the removal of abscessed teeth, illustrate well the importance of constantly close correlation between the dental and the other departments of a general diagnostic clinic

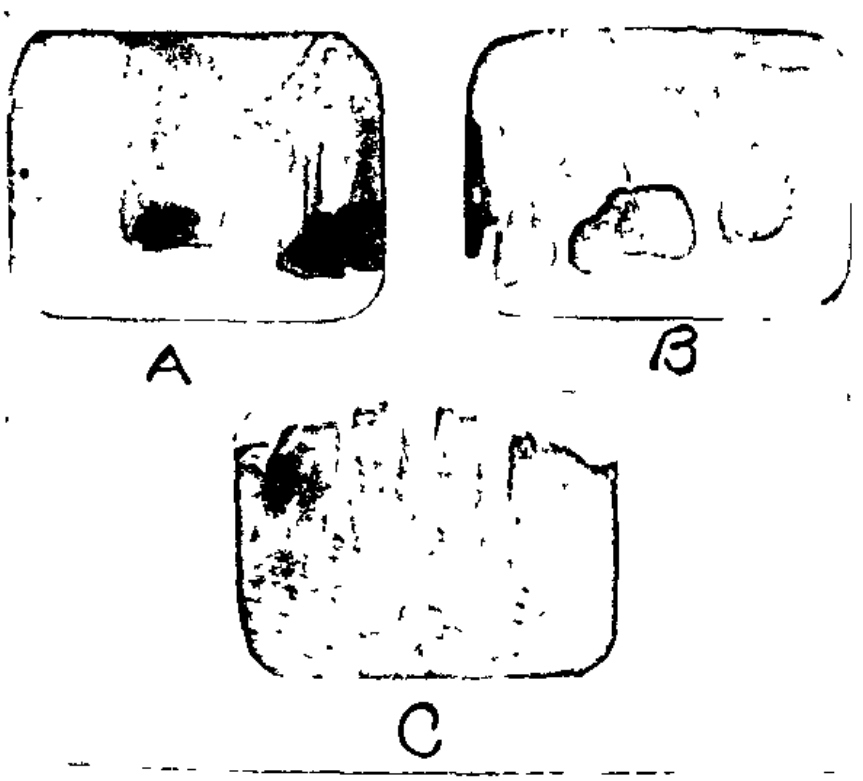

FIG. 400.—A, Abscessed upper left second bicuspid. B, Apical infection, upper right second bicuspid. C, Resorption of the alveolus, lower anteriors.

Case I.—The patient, a married woman fifty-two years of age, came to the Clinic for the relief of pain and swelling in the right elbow which had persisted for six months, with extension to the shoulder during the last five days. There was no significant indication in her previous history except for

a fall a few days before the onset of the pain in the elbow, and the physical examination elicited nothing of importance except for the local condition The temperature was 98 6° F., blood-pressure 160/96 Examination of the right arm showed a diffuse swelling in the region of the deltoid muscle and marked tenderness on pressure over the lower portion of the deltoid region, with limitation of abduction and of both external and internal rotation The diagnosis of an acute subdeltoid bursitis was made which might have been due to the fall, but a search for possible foci of infection was made Nothing was found in the lungs, throat, nose, or abdomen.

Examination of the teeth, however, showed an abscess of the upper left second bicuspid with resorption of the alveolus in the lower anteriors (Fig. 400) Physiotherapeutic measures were instituted at once, and the infected teeth were extracted Ten days after the extraction, although there had been no intervening physiotherapeutic treatments, the patient's condition had markedly improved There was still some discomfort around the upper end of the right radius, but no swelling or redness, and there was quite a free range of movement about the right shoulder-joint

Case II.—The patient, a toolmaker, twenty-four years of age, came to the Clinic because of a painful right shoulder which had troubled him for the preceding eleven months This trouble was apparently initiated by a right palmar infection, in the course of which some soreness had developed in the right axilla During the course of this infection he contracted pleurisy with pneumonia and was ill in bed for seven weeks, during which time his right shoulder became swollen and very painful. The shoulder movement had been limited ever since that time and the joint had ached constantly

Physical examination showed an acneiform eruption over both shoulders and the face The tonsils had been removed, and the patient stated that his teeth had been *x*-rayed and one infected tooth extracted There were no suspicious findings with the exception of the local signs about the shoulder-joint, where there was diffuse swelling, but no redness There was tenderness on pressure and a slight limitation of movement in all directions, and definite fluctuation over the posterior portion of the joint The *x*-ray which accompanied the patient, who was referred to Dr Dickson of the orthopedic department by Dr. W M Bucher of Cleveland, showed marked destruction of the head of the scapula with some thickening of the cortex of the upper third of the humerus

The patient was sent to the hospital, where the shoulder-joint was aspirated and about 3 c c of pus obtained, the culture from which showed the presence of staphylococci

At first it was thought that this was primarily a tuberculous condition, and *drainage of the joint was instituted* Four weeks later the wounds had healed well, the patient appeared to be gaining in weight and, in general, was feeling very much better

By that time it appeared that this was an infectious arthritis due to a low-grade pyogenic infection rather than to tuberculosis, and it seemed advisable to carry further the search for a possible focus *x*-Ray of the sinuses was negative, the abdominal examination gave negative results nothing was

found by examination of the nose, throat, or ears. A dental examination, however, showed that the upper right first bicuspid, which had been crowned, showed no evidence of canal fillings and there was a decided apical shadow (Fig. 401). The crown was removed and the pulp was found to have been destroyed. The extraction of this tooth was advised and was done elsewhere.

Since then there has been continuous improvement. The shoulder still discharges a little, but there is little pain, and the condition will probably be terminated by a later operation for arthrodesis of the joint

Fig 401.—Crowned upper right first bicuspid showing suspicious shadow at apex.

The point of note in this case is the identification in the apex of a tooth of the probable focus which kept alive an infection which may or may not have originated primarily by extension from the palmar infection.

Case III.—This patient, a boy nineteen years of age, was struck over the sternum in the course of a football game. He played through the game, but severe pain developed during the night, and on the following day he was taken to a hospital, where *x*-ray findings were reported to be negative. About a week later a swelling appeared at the site of injury, which gradually increased in size for about three weeks, when it was opened and a quantity of pus was evacuated. The pain disappeared and the patient had had no more local discomfort, but he continued to lose weight.

Physical examination showed a very pale, frail appearing youth showing evidence of recent loss in weight, weight at this time 146 pounds Examination of sinuses and abdomen were negative. There were some badly decayed teeth, but no other external evidence of dental pathology. The sinus over the sternum was still discharging, but no destruction of bone or cartilage was demonstrable by direct examination or by *x*-ray. Examination of the heart showed occasional premature ventricular beats, but nothing to account for the continued malaise and loss of weight. Chest examination gave negative findings The patient was referred to the orthopedic department, where physiotherapeutic treatments and exercises were given

Twenty days after his primary examination at the Clinic he was referred to the dental department, where apical infections of the lower right and

lower left first molars were found (Fig 402), and these teeth were extracted. No further physiotherapeutic treatments were required.

In this case improvement was certainly initiated by the physiotherapeutic measures under which the boy gained 26¼ pounds The query that is suggested, however, is, Would that improvement have been permanent in the presence of the well-defined foci in the mouth?

Fig. 402.—A, Apical infection, lower right first molar. B, Apical infection, lower left first molar.

Case IV.—This patient, a married woman thirty-seven years of age, was referred to the Cleveland Clinic on April 20, 1923 with the following history of illness during the preceding two months. About the middle of February she had experienced aching sensations distributed over the whole body, without any accompanying symptoms This passed, but after about a week the aching returned and she stayed in bed for four days, during which she had considerable fever. About ten days later there was another attack of general aching and she was in bed for six days. At this time the glands in the neck and her throat were swollen; the patient vomited and had a high fever This attack was diagnosed as "grippe." About a month before she came to the Clinic she had pleurisy in the lower right chest and also developed a slight jaundice. About a week later she went to bed with "rheumatism" At that time the flesh was sore in various regions and there was slight swelling of the knees. At the time of the consultation she had sharp pains in different parts of the body, was very nervous, and had a slight headache and a slight cough. She reported that she was very constipated and that she found it difficult to get to sleep at night She thought she had lost some weight

Physical examination revealed nothing abnormal with the exception of pyorrhea and an abnormal cardiac condition indicated by a presystolic thrill ending in a systolic impact over the apex The pulse was 104, blood-pressure, diastolic 124, systolic, 74, temperature, 98 2° F

The laboratory findings were as follows:

The *blood-culture* showed two small colonies of Streptococcus viridans

Blood-count: Red blood-cells, 4,050,000; white blood-cells, 9000; hemoglobin, 80 per cent.

Differential count (200 cells): Polymorphonuclears, 75 per cent., eosinophils, 1 per cent.; small lymphocytes, 22 per cent.; transitionals, 2 per cent

Character of red blood-cells normal.

The *urine* was acid in reaction; specific gravity, 1024, very slight trace of albumin, no sugar, very slight trace of indican; 3 to 5 white blood-cells to the microscopic field, an occasional hyaline cast, a moderate number of threads of mucus, and an occasional cylindroid.

Three months later, after several intervening visits, the patient was referred to the dental department for examination, which revealed (1) abscessed lower right second molar; (2) abscessed upper left lateral, (3) apical absorption of upper left cuspid and first bicuspid (Fig. 403). The

Fig. 403.—A, Abscessed lower right second molar B, Apical absorption of cuspid and first bicuspid.

abscessed teeth were extracted and eleven days later the patient reported that she was feeling better and stronger. Two months after the extraction she was still feeling quite well with the exception of palpitation. At that time her pulse was 80; temperature, 98.2° F ; blood-pressure, 120/70.

Case V.—The patient, a man, radiographs of whose teeth are shown in Fig 404, was referred to me by Dr. S. T. Forsythe in the belief that the iritis from which he had been suffering for some time must be an extension from some focal process elsewhere.

Examination of the teeth as indicated by the x-ray plates showed in the upper right third molar region an impacted malposed tooth, absorption of the alveolus involving the apical third of the lower anterior teeth; absorption of the alveolus in the upper anterior region; absence of pulp in the upper right central teeth, and an advanced stage of pyorrhea of all the teeth. Although it was hoped that treatment would save some of the infected teeth, the patient

did not feel that he could give the time for this, so all of the teeth were extracted, the extractions being accomplished between April 25th and July 2d.

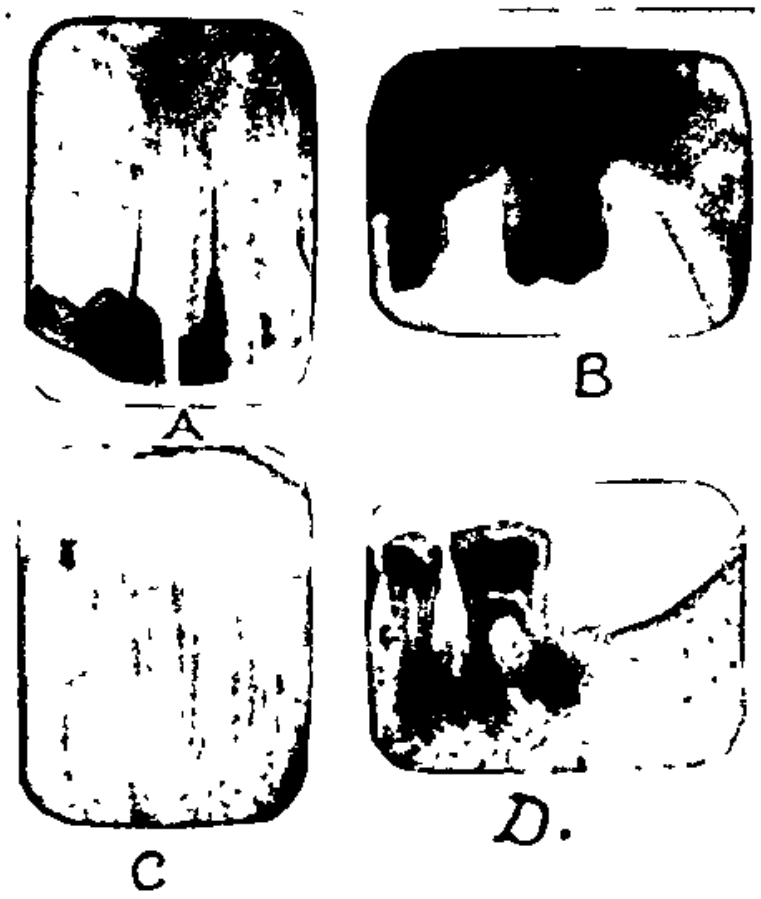

Fig 404.—A, C, D, Absorption of alveoli which was more or less general. B, Impacted malposed molar.

Dr Forsythe reports today (July 21st) that the iritis has completely disappeared.

Several similar cases of eye infections have been referred to us which have cleared promptly after the extraction of infected teeth

With the exception of Case V these cases show the following point in common, viz , that in each the condition for which relief was sought had an apparently well-defined cause. In the first a fall; in the second a palmar infection; in the third a neurasthenic condition following a heavy blow and resultant local abscess; in the fourth endocarditis with streptococci: septicemia. In each an apical infection was demonstrated. While it is impossible to

state exactly what rôle was played by the apical infection in any of these cases, on the other hand, it is reasonable to assume that whether or not it was a primary cause of the subdeltoid bursitis, of the suppurative arthritis, of the loss of weight and general malaise accompanying and following the development of the sternal abscess, nevertheless, it was certainly a contributing factor, and its elimination must have been an essential factor in the final results.

It would appear, therefore, that the examination of the teeth might well be included in the routine examination, not only in those cases in which a general census is indicated by the lack of any apparent cause of the condition but also in all arthritic conditions, in eye infections of uncertain etiology, and in cases in which general malaise follows a pyogenic lesion anywhere. It may be added that in cases of cholecystitis also abscessed teeth may be an important etiologic factor. In such cases treatment of the gall-bladder alone without the removal of the source of the offending organisms is obviously of no avail.

C. L. HARTSOCK

DEPARTMENT OF INTERNAL MEDICINE

MIGRAINE

HEADACHE is a very common and a very distressing symptom in a large number of people who otherwise claim to be well and certainly appear so, except during the attacks of headache. In some these attacks are of brief duration, while in others they are so protracted and so severe as to be a serious economic handicap.

There are numerous causes for headache. It is probably second only to distress in the stomach in sounding a warning of some deranged body function. This discussion, however, will be limited to a consideration of a peculiar and as yet unexplained syndrome in which headache is the main feature—migraine, commonly spoken of as bilious or sick headache.

I speak of migraine as a syndrome and not as a disease, because I feel that all the objective and subjective features of this disturbance are the results of some form of intoxication superimposed on an impaired nervous system

The following clinical examples of the syndrome will serve to illustrate this conception of the nature of migraine. It may be well first to present a typical case and then to discuss several cases that illustrate the more unusual features of the syndrome.

A housewife, forty-six years of age came to the Cleveland Clinic seeking relief from repeated sick headaches which for twenty years had occurred regularly once a week. On Thursday or Friday of each week the patient would experience a feeling of general lassitude, and shortly thereafter would notice a slight unilateral headache. Approximately coincident with the time of the onset of the headache her vision would become slightly blurred, and in several attacks she had seen zigzag flashes of light. These eye symptoms were of short duration. The head-

ache would gradually increase in severity, until after four or five hours it was described as "splitting" and "unbearable." At this point vomiting would begin, with a slight amelioration of the headache. The vomiting would last about six hours, or until a "very dark green, bitter bile" was brought up, when the headache would cease. The patient would be prostrated and obliged to remain in bed from two to four days, during which time she ate very little or nothing. During the remainder of the week she would feel perfectly well. Four years before she had consulted a very able diagnostician, who, on account of a suggestive family history of lues, in spite of a negative physical, blood, and spinal fluid examination, made a diagnosis of cerebrospinal lues, and gave her vigorous antiluetic treatment, without any effect

In addition to a family history of lues on both sides, there was a very characteristic history of migraine on the maternal side antedating marriage.

A thorough physical examination, including a-rays of teeth and sinuses, refraction of the eyes, and blood Wassermann, was normal The patient showed no signs of beginning menopause

She was placed on the routine treatment I shall describe later, and immediately the headaches stopped and have not returned after one year, in spite of the fact that the patient was laid up for one week with a fibrinous pleurisy and for three weeks with erythema nodosum. There are still no signs of the menopause I mention this fact because frequently in women attacks of migraine cease at this time without any form of treatment

This case has presented the most severe and the most classical symptoms, and has yielded the most satisfactory results of any in the group of so-called typical cases which have come under *my observation* It may be well to present here an analysis of these cases before discussing the treatment which proved so effective in the severe case which we have described.

Migraine attacks both sexes, but occurs slightly more often in the female sex. Most of the cases in this series, which includes between 50 and 60 cases, first consulted a doctor between

the ages of twenty-five and thirty-five after having had attacks for periods varying from one to twenty years The youngest patient in this group was twelve years of age, although migraine not uncommonly attacks children as young as five or six years of age. The oldest of these patients was seventy-two The attacks tend to disappear in later life, and in women especially at the time of the menopause, as mentioned above. Many patients over fifty years of age give a very definite history of attacks of migraine in earlier years, mentioning their relief and delight that they are no longer troubled. By far the greater number of the cases in this group were of the intellectual type, but I believe that when we are able to classify the disease correctly according to its etiology, whatever that may prove to be, it will be found to be much more common in the laboring class than we now suppose, because in many of these cases the headache will be absent, the diagnosis being made on the basis of the prodromal symptoms and symptoms referable to the gastro-intestinal tract especially, as illustrated by one case which will be described later. At the present time, as the diagnosis of migraine is rarely made in the absence of headache, I believe that many cases which belong to this syndrome are excluded from the statistics.

The attacks are periodic—and this point is very important in establishing the differential diagnosis—occurring usually at least once a month. In women the pelvic organs are nearly always believed to be involved because of the close association of the attacks with the menstrual function. The headache is very severe; in 70 per cent of our cases it was unilateral, remaining always on the same side in 20 per cent. and changing from one side to the other in different attacks in 50 per cent.; in 30 per cent. of our cases it involved both sides. In general the pain begins in the temples and with slowly increasing force reaches a maximum intensity, which in severe cases is prostrating. It is variously described as boring, throbbing, gripping, splitting, or blinding.

A prodromal symptom is almost constantly present and may occur as much as a day or only a few minutes before the onset

of the headache This prodromal symptom may be a sense of general well being which usually is experienced the day before the attack, when the patient feels exceptionally well; the mind is clear and he is able to do an unlimited amount of work; an increased appetite usually accompanies this feeling. Of just about equal occurrence is a prodromal feeling of lassitude and anorexia. Indefinitely located pain in various parts of the body is a common prodromal symptom, the abdomen being a common site for this type of pain. Numbness or tingling of the nose, ears, or extremities, associated with a feeling of general weakness is not uncommon. Aphasia is often associated with this type of prodromata

Eye phenomena are very common during the attack. In my experience temporary blindness or blurring of the vision in one or both eyes occurs more commonly than the classical and almost pathognomonic zigzag lights, the so-called "fortification spectra" In this series 35 out of 60 experience eye phenomena, while only 5 of these had fortification spectra. These eye phenomena are pictured in nearly every text-book, and I shall not discuss them further here except to say that very often they give the patient more concern than any of the other features of migraine, so that an oculist usually sees quite a number of cases of migraine each year.

Gastro-intestinal symptoms frequently follow the headache. Of these, anorexia is the most common and is almost invariably present Nausea is very common, and the headache frequently terminates with vomiting of the so-called "bitter bile." Diarrhea often occurs on the day following the headache. These gastro-intestinal disturbances often explain the presence of an appendectomy or cholecystectomy scar in these patients without accompanying relief of symptoms

The patient is prostrated and usually is obliged to stay in bed for from one to seventy-two hours. He seeks a quiet, dark place, and prefers to be left alone. The old saying, "misery loves company," does not apply in this instance. Recovery is uneventful and rapid, and unless the migraine is complicated with some other disease the health is good between attacks

In reviewing the past history of these patients it is impossible to establish any relation between the migraine and any previous illnesses or habits. The family histories were very incomplete, but a history of the existence of a similar condition in one of the immediate relatives was secured in 50 per cent. of our cases, this percentage being sufficiently high to justify the belief that heredity is the most important etiologic factor thus far determined.

In addition to migraine, alcoholism, nervousness, insanity, and epilepsy were frequently mentioned in the familial history.

It has been very interesting to find that women whose attacks occur only at the menstrual periods are frequently free during pregnancy and the first few months after childbirth. On the other hand, one patient whose attacks were not related to the menstrual periods was very much worse during pregnancy

A typical case, then, may be summarized as consisting in a periodic "explosion" in the body which produces: (1) various symptoms characterized by nerve or vascular phenomena, (2) headache, (3) gastro-intestinal symptoms.

With these three phases of typical cases in mind, several cases may be cited which ordinarily would not be diagnosed as migraine, but which I am unable to place under any other classification, and believe to be closely related to or similar to migraine

While talking to a visiting physician one day he put his hand up to his eyes and said they were blurred so that he could not see anything distinctly. He described the presence of zigzag lines which he traced in the air for me. The condition passed off in two minutes and was not followed by any further disturbance He said these attacks occurred every two months and that no other symptoms were ever associated with the visual disturbance. Needless to say, this case was not treated.

Another case presents a dissociation of symptoms which I have seen in no other instance. A lawyer, fifty-five years of age, with a very active practice, consulted a surgeon because of blurring of the eyes, headaches, and attacks of nausea and vomiting. These symptoms, however, occurred separately and

appeared to bear no relation to each other. The blurring of vision which was similar to that in the case just described, but without flashes of light, lasted for half an hour. This visual disturbance was never followed directly by headache, but a severe unilateral headache would develop several days or a week later. These attacks came periodically about once every two weeks and, in addition, about once a month the patient would have a spell of nausea and vomiting not associated with pain.

A careful clinical examination and a radiographic examination of the sinuses, kidneys, and gastro-intestinal tract revealed nothing but a suspicious shadow in the gall-bladder region. An exploratory operation revealed one large stone and a mildly infected gall-bladder, which were removed. The patient was given instructions as to diet and the care of the bowels, and after several months of rest he returned to work. The attacks of headache and of blurring of vision continued as before. The gastric symptoms were very much relieved, but not entirely so. The treatment to be described was prescribed, but I have had no reports as to the result.

Another case I am following with great interest to see whether migraine develops later. A boy three years of age, with no family history of headache, epilepsy, or neurasthenia, began to have attacks of headache and malaise associated with fever (103° to 105°F.), with nausea and vomiting after twelve hours, the latter symptoms persisting two days, after which the child rapidly recovered. His health was good between these attacks, which came on periodically about every six weeks until the child was six years old. Examination between attacks showed a normal child. During an attack his complexion was rather pale and pasty and he was extremely nervous and irritable. The abdomen was always soft and no tenderness could be elicited. The leukocyte count was never over 9000 and there was no increase in the polymorphonuclear and neutrophil counts. There was some constipation, when the stools were rather offensive, the bowels being relieved by enemata. At the age of six the carbohydrate intake was greatly restricted, and the child was given a small amount of rhubarb and soda mixture every week, with resultant

complete relief from the attacks for two years, except for an attack at Christmas, when it was difficult to enforce the prescribed diet. I have seen 4 other children with similar disturbance, all of whom improved under similar treatment.

Another atypical case was that of a young man twenty-three years of age, doing physical work. He was apparently in good health except for the fact that about once a month after a day during which he felt exceptionally well he would suddenly become very tired, listless, unable to concentrate, and dizzy, but with no headache or vomiting. He had found that after the attack developed he obtained immediate relief from calomel and saline, but he had never tried taking these as a prophylactic measure. In this case the symptoms which resembled those of migraine were undoubtedly due to an auto-intoxication. The question raised in my mind was whether this would be definitely a case of migraine with headache if the occupation and temperament of the patient were different, that is, if his work were mental instead of physical, and if he were of a nervous temperament.

Another and a most interesting case was that of a girl fifteen years of age, who since the age of eight had been having migraine-like attacks every month. These began with a numbness and tingling of the right hand, which slowly traveled up the arm, requiring about fifteen minutes to reach the shoulder. The tongue then became thick and aphasia developed. The vision became blurred and shortly after this headache would begin above one of the eyes, the attacks then progressing as in a typical case. The patient would be prostrated for two or three days. Nothing abnormal was found on examination except a moderate chlorosis. Three months before I saw her the attacks had occurred every two weeks. Under the usual treatment the intercurrent periods were lengthened first to a month and then gradually to six months, the attacks being usually less severe than formerly, although occasionally one would be extremely severe. In this case there was no familial history of headache. The patient has recently been married and I have lost trace

of her, but I hope to find out some day the effect of pregnancy on the recurrence of the attacks.

We are still as much in the dark as ever regarding the etiology and pathology of migraine. Numerous theories have been formulated to explain the symptoms, none of which satisfactorily explain all the features of the syndrome. The most common conception is that all the symptoms are due to vasomotor changes, the prodromal symptoms being due to a spasm of the cerebral artery, and the headache and gastro-intestinal symptoms to the relaxation following the spasm which results in increased intracranial pressure This theory is very plausible, especially as examination of the eye-grounds during an attack has frequently shown a spasm of the retinal artery. Another very plausible theory is that migraine is due to a primary disturbance of the cerebral cortex, with secondary vasomotor phenomena Among other less plausible theories may be cited that which suggests that the symptoms of migraine are due to a periodic functional swelling of the pituitary gland, especially at the menstrual period, with resultant pressure on the optic tract and a general increase in intracranial pressure; another accounts for migraine by assuming an occlusion of the foramen of Monro on one side, with resultant increased pressure, and recently there has been an attempt to place migraine in the group of anaphylactic phenomena along with hay-fever, asthma, urticaria, etc.

Personally, I believe that migraine is the result of some irritating lesion or toxemia which produces an accumulation of afferent nerve discharges into a highly strung and specially sensitized cortex, with a final resultant violent explosion of the perturbed cells which suddenly releases the afferent accumulation just as static electricity is released by touching the charged body This conception in general corresponds with the second theory cited above

In support of this conception may be cited the numerous reports of cases which have been cured by the removal of some very minor defect, such as astigmatism, nasopharyngeal deformity, by the removal of a chronic appendix, or the correction of some slight gynecologic disorder. Any one of these in itself

would seem a remote cause unless we realize that each has been constantly irritating the cortex by continuous subconscious afferent impulses. I believe that very frequently the irritative impulses cause metabolic disturbance in the gastro-intestinal tract. Gowers, in particular, has called attention to the fact that gout and migraine are very closely associated and are probably related to each other in some way. But while it is definitely known that gout is due to faulty metabolism, with resultant excess deposition of urates, no chemical substance has ever been found to be a causative factor in migraine; many substances have been suspected, but no conclusive proof regarding any has been found.

There is no doubt that heredity plays a very important part in the etiology of migraine If our theory is correct, the part heredity plays is to produce a sensitized nervous system. That this is the case is suggested by the fact that in a given case of epilepsy or of migraine the disease itself may not appear in the ancestral history, which, however, does include some such condition as neurasthenia, alcoholism, etc. The significance of these is hard to trace, however, if they are mendelian characters.

As for the relationship of migraine to epilepsy, there has been much disagreement, although on account of the many similar features—viz., heredity, periodicity, and the similar prodromal symptoms—it has been considered by some that epilepsy is the motor and migraine the sensory manifestation of the same fundamental disturbances.

A few cases are reported in the literature in which definite migraine with optic phenomena has passed into epilepsy characterized by the same eye phenomena as prodromal symptoms.

A case of epilepsy has been reported in which for several years the epilepsy was supplanted by migraine which, in turn, reverted to epilepsy. However, in spite of these cases in which migraine and epilepsy have apparently been transformed the one into the other and in spite of other similarities between the two conditions, on the other hand, there are such wide variations between them, especially in the mental status of the patients, that today it is generally believed that migraine and epilepsy

are distinct entities each of which is characterized by a cortical explosion; and that, although both may be present in the same person, the conditions are not directly related, a conclusion which should reassure every migraine sufferer who may have heard or read of this relation.

The diagnosis of migraine is usually easily determined, although, unlike many other diseases characterized by periodic attacks, it is much more easy to make the diagnosis from the history than when seeing a patient in an attack for the first time, when the extreme prostration and suffering may suggest an acute gastro-intestinal condition. Inquiry should always be made regarding the recurrence of previous attacks, the character and periodicity of which should be carefully reviewed, as this history will usually give a better insight into the nature of the attack than the examination of the distressed patient who will seem to be going through more than a functional disturbance.

On the other hand, although the diagnosis is, in the main, based upon the history, a very complete examination of the patient is extremely important if we are to relieve him instead of merely giving him a correct diagnosis to take away with him, as too frequently happens. This is the real reason why many of these patients go on for years without relief from their suffering Nearly all of them have consulted not only one but many doctors, and in many cases the diagnosis has been correctly made; but in reviewing our series of cases it has appeared that but rarely has a determined effort been made to relieve the condition While it is true that migraine leaves no bad effects and does no harm other than to discommode a patient for a part of the time, nevertheless it certainly does hinder and sometimes seriously impede his economic progress, and for this reason alone every possible effort to secure relief should be made. I may say that there are no more grateful patients than such of these sufferers as have been relieved of their attacks.

The examination should be especially directed to the discovery of errors of refraction, pathologic nasopharyngeal conditions such as deflected septum, polypi, infected tonsils and adenoids, pathologic dental conditions, flat chest with poor

aëration of the lungs, visceroptosis, and pelvic and genital abnormalities. Chronic appendicitis and chronic cholecystitis should be looked for, but it should be borne in mind that sometimes these organs have been removed without any resultant relief from the gastro-intestinal symptoms accompanying the attack of migraine. The term "bilious headache" used by the laity is certainly misleading, and I believe it is partly responsible for the extent to which the attention has been focussed on the biliary tract.

The treatment of migraine is divided into two phases: the relief of the attack when it occurs; and general treatment to prevent or decrease the severity and frequency of the attacks.

When an attack of migraine has been fully inaugurated but little can be done for the patient except to make him as comfortable as possible until it subsides. In the severe cases the patient should be put absolutely to rest, preferably in a darkened, cool room. Food will be automatically discontinued. If the patient is vomiting a gastric lavage with warm soda water is useful. If vomiting has not started, an enema or brisk saline purge, or both, can be given. A hot mustard foot-bath is sometimes helpful. Unless the patient is seen early in the attack drugs are of little help. If taken at the first warning of an attack they sometimes abort it, but the dose must be large, as mentioned later. Morphin should be withheld except in exceptionally severe cases, or in emergencies in which it is necessary for the patient to carry on some essential task for a few hours.

The real service to the patient comes in the prevention of the attacks, and to accomplish this requires all of the ingenuity of the physician, for it is a difficult task. If treatment is attempted there must be thorough co-operation between the patient and and the physician. The patient should be warned, first, that if relief is to be obtained treatment must be continuous unless the correction of some simple abnormality, such as adenoids or eye strain, is all that is indicated; and second, if relief is not obtained after a fair trial not to become discouraged, but to return to the physician in order that the form of treatment may be changed. The multitude of therapeutic measures listed in

the literature attests the fact that all patients will not respond to any single kind of treatment, but that some will probably respond to each. It thus remains for us to hold our patient until either by good fortune or by scientific control we strike the right combination. I believe very firmly that there are but few cases which will not respond wholly or in part if we are persistent and not discouraged after the first failure

I usually start the patient on the following routine:

(1) *Correction of All Organic Defects.*—This includes correction of refractive errors, the removal of nasal obstructions or pressure, the treatment of infection of the sinuses and the removal of diseased tonsils, the removal of abscessed teeth, the filling of cavities, and the restoration of masticating efficiency.

Postural exercises are given to develop the chest and to correct visceroptosis, protruding abdomen, and lumbar lordosis. The full importance of these would require a chapter in itself. It is enough to say here, however, that the patient must gain weight and restore the abdominothoracic space for the organs by raising the diaphragm and increasing the tone of the muscle in order to secure better function of the circulatory and digestive organs

Female pelvic abnormalities should be repaired, and in the male particular attention should be paid to cryptorchidism and phimosis

Flat-foot should not be overlooked.

(2) *Correction of Mode of Living.*—Sedentary people are made to exercise, and people who lead a very active life with great nerve strain are advised to modify their activity as far as possible, especially those women whose lives are principally occupied with either entertaining or being entertained.

Eight hours of sleep should be the rule, but it is important that the amount of sleep should not be excessive. Rest after the midday meal is an excellent habit to develop; exertion to the point of fatigue should always be avoided.

The habits of children, in particular, should be carefully regulated

(3) *Regulation of Diet.*—There is a widely diversified opinion

as to the rôle played by diet in the causation of migraine. Both carbohydrates and proteins have been incriminated, and in a few cases even the fats. I usually put the patient on a well-balanced diet, avoiding excess starches, proteins, and milk, and allowing plenty of vegetables, fruits, and butter fat The diet must be modified to suit other conditions which may be present, such as hyperacidity, visceroptosis, etc. The following is a good standard diet:

Broth and creamed soups which are not rich in spices, condiments, or meat extracts.

Veal, lamb, mutton (broiled or boiled), rare roast beef, bacon, steak

Chicken, turkey, squab (boiled, broiled, or roasted)

Raw, soft-boiled, or poached eggs.

Blue pike, white fish, bass, haddock, halibut, trout, or mackerel.

White potatoes (mashed, boiled, or baked), peas, string beans, asparagus, spinach, cauliflower, squash, carrots, celery, beets, macaroni and spaghetti, rhubarb, lettuce, cream cheese, canned tomatoes

Any cereal.

Oranges and bananas; cooked pears, peaches, prunes and apples; berries, and melons

Puddings—rice, cornstarch, tapioca; cup custard, gelatin, and vanilla ice-cream.

Milk and cream; cocoa, weak tea, and coffee sparingly; buttermilk.

Any bread except hot breads.

Simple lettuce salad with oil.

If there is no response to this diet, the starches are eliminated entirely, and later the proteins and fats in the order named if still there is no relief. I have found better results from carbohydrate reduction than from protein reduction.

(4) *Care of the Bowels.*—This is extremely important. General measures for the care of constipation should be instituted when necessary, such as the formation of a regular habit of evacuation. Bulky foods such as bran, fats such as olive oil and butter when not contraindicated by obesity, and fruits are advised. Agents which prevent drying of the stool, such as mineral oil and agar, are prescribed.

Spastic colons should be treated with sedatives and antispasmodics. Atonic colons should have massage and electric stimulation.

In addition to these general measures a routine cathartic of

calomel followed by saline should be given every two weeks if the attacks occur as frequently as that, or every month when they are of less frequent occurrence.

High colonic enemata when the treatment is started, and daily for two weeks, often yield unexpectedly good results.

(5) *Drugs.*—Every physician has his pet prescription, but drugs alone are worthless. After the headache has begun the antipyretics, such as aspirin, pyramidon, phenacetin, given alone or combined with codein are most frequently used. The dose should be large to be of benefit The bromids are probably the most reliable drugs for preventive use. From 5 to 10 grains may be given three times daily together with tincture of hyoscyamin or tincture of valerian Tincture of belladonna and atropin sulphate solution have been used, with good results in selected cases, especially in those with spastic colons. In debilitated and anemic cases iron, arsenic, and strychnin are indicated

Many cases have gastric hypersecretion, and in these the antacids are particularly beneficial. Ox bile and pancreatic extract have limited uses

(6) *Psychotherapy.*—Many of these patients are very nervous and highly strung, and often it is necessary to inquire rather carefully into the home conditions in order to eliminate as far as possible small annoyances which may be constant sources of irritation Constant encouragement should be given these individuals.

Prognosis —A guarded prognosis as to complete recovery should be given in every case, as the results of any form of treatment are always in doubt until it has been tried. The patient should be reassured, however, as to the benign nature of the trouble and, as previously mentioned, he should be instructed to return for further advice if the first attempt at treatment is unsuccessful The older the patient, or in the case of women, the nearer the climacteric, the better the chance of getting a good result. Nearly every case can be helped in some degree and the gastro-intestinal symptoms in particular can be alleviated, a result which in itself alone is worth securing in many cases

JOHN TUCKER

DEPARTMENT OF INTERNAL MEDICINE

PROGRESSIVE LIPODYSTROPHY ASSOCIATED WITH MALABSORPTION OF FAT

(PRELIMINARY REPORT)

IN September, 1907, G. H. Whipple[1] reported an unusual case of progressive loss in weight and strength, associated with frequent stools containing large quantities of neutral fat and fatty acid, indefinite abdominal pains, and arthritis. The necropsy findings revealed enlarged intestinal villi, the lymph-spaces of which were filled with large masses of neutral fats and fatty acids; and also an infiltration of the interglandular tissue by large mononuclear and polynuclear giant-cells. To this clinical and pathologic picture he applied the term "intestinal lipodystrophy."

A fresh interest in this curious syndrome was aroused by H. L. Blumgart[2] who reported 3 cases under the title Three Fatal Cases of Malabsorption of Fat. In these patients the condition was marked by emaciation, frequent fatty stools, anemia, and absence of free hydrocholoric acid in the stomach after an Ewald meal. The necropsy findings in each case revealed a striking absence of fat and intra-abdominal fat, in particular, together with enlarged mesenteric lymph-nodes. In addition, Blumgart found lymphoid hyperplasia of the small intestine and a minute granulation of the mucosa extending from the duodenum toward the ileocecal valve. As in Whipple's case, phagocytes were present in the submucosal lymphatics, which were filled with fat droplets. In Blumgart's third case the lower jejunum revealed many rough, circular, and indolent ulcers, with an accompanying megacolon. We are of the opinion that the case reported below presents sufficient clinical and laboratory evidence

to be classified in the same group as the cases of Blumgart and Whipple.

Case History.—The patient, a white youth eighteen and a half years of age, a farmer by occupation, on May 19, 1924 entered the Cleveland Clinic for examination because of weakness and loss of weight. There was no familial history of cancer, insanity, or of chronic illness. The patient had had scarlatina at the age of four, mumps at six; pertussis at eight, and an illness which he stated was diagnosed as malaria at the age of eleven when he was living in Missouri. He presented no other history of illness with the exception of an attack of influenza five years before, which was followed by a very slow recovery, but was not followed by encephalitis or any other complication, and an attack of measles one and a half years before. His vision was good, his hearing fair, he had never had any dental trouble or any soreness of the mouth, tongue, gums, or throat, there had been no chronic cough, no shortness of breath, no swelling of the eyelids or feet; he had never noticed any thoracic or abdominal discomfort and never had jaundice, "indigestion," or nocturia. He slept normally at night and had no abnormal tendency to somnolence during the day. He suffered no undue fatigue from ordinary activities of his occupation. The only interesting feature in his personal history was his weight record, which was as follows:

Age, years	Date	Weight, pounds
15½		194
17	April, 1923	175
17½	August, 1923	140
18	February 1, 1924	155
18½	June 6, 1924	115

Present Illness.—During the last three years the patient had noticed a gradual loss of weight, which during the last year and a half had been accompanied by increasing weakness, making it progressively more difficult for him to carry on his work. During this period, however, his appetite had been excellent, his bowels had moved regularly and abundantly once or twice daily. The excreta had been rather light in color and had presented no evidence of the presence of parasites. At no time had the patient experienced any pain or headache, medical consultation at this time being entirely due to the anxiety of his parents because of his emaciated appearance.

Physical Examination.—The patient was a well-developed boy of alert bearing. His face, neck, arms, and hands were well tanned from exposure and there was a band of brownish discoloration about the belt line. The entire body showed a strikingly emaciated appearance—sunken cheeks, wasted extremities, prominent rib markings, and thin-walled abdomen, which was due to the notable absence of subcutaneous fat over the entire body. No muscular atrophy, however, could be detected and there was only a moderate weakening of the legs, arms, and trunk.

The skin had a harsh feeling like that of gooseflesh, with diminished tur-

gor and loose subcutaneous tissue. The pupils showed a normal reaction, the teeth were sound in appearance, and the tonsils atrophic. There was no glossitis or lingual ulceration. Examination of the lymph-glands and spleen revealed no hyperplasia. Expansion of the chest was normal There were no râles, but there was slightly impaired resonance, with prolonged harsh breath sounds at the right apex, which were regarded as due to a retracted apex resulting from a healed tuberculous lesion The heart was normal in size and there were no murmurs, the pulse was regular and rhythmic—rate 56. The blood-pressure was—systolic 100, diastolic 76. There was no thickening of the palpable blood-vessels. The mouth temperature was 96.2° F. A roentgenogram of the lungs was normal Fecal masses in the colon were visible through the thin walls of the abdomen and were readily palpable, the liver and spleen were not palpable and no tumor or free fluid could be demonstrated. Inspection and palpation revealed no abnormality of the genitalia or rectum. The patella and Achilles' reflexes were equal and active The abdominal reflexes were present. The Babinski, Oppenheim, and Romberg signs were absent. Muscular co-ordination and tonus were normal.

Laboratory findings (May 19, 1924) *Urine*, acid reaction; specific gravity, 1018, albumin, very faint trace, no sugar, microscopic examination showed presence of white blood-cells and a few epithelial cells

Blood Red blood-cells, 4,600,000; white blood-cells, 6700, hemoglobin, 75 per cent.

Differential count (200 cells): Polymorphonuclears, 54 4 per cent ; small lymphocytes, 44.5 per cent.; eosinophils, 1 per cent. Character of red blood-cells normal; no malaria plasmodia seen.

July 5, 1924. Red blood-cells, 3,680,000; white blood-cells, 6600; hemoglobin, 80 per cent.

Differential count (200 cells): Polymorphonuclears, 37.5 per cent.; small lymphocytes, 56 per cent.; eosinophils, 4 5 per cent.; basophils, 2 per cent.; slight anisocytosis

Blood chemistry: May 19, 1924: Sugar, 87; urea, 42; creatinin, 1.3; chlorids, 515 mg. per 100 c c.

June 9, 1924: Sugar, 86, urea, 21; creatinin, 1 1; chlorids, 595 mg. per 100 c c. Sugar tolerance curve normal.

July 8, 1924· Sugar, 83 mg. per 100 c.c ; plasma acetone negative

Basal metabolic rate, minus 25 per cent. on May 19, 1924.

Ewald test-meal: Free hydrochloric acid, 26; total acid, 64; lactic acid, 0, bile, 0; blood, 0; microscopic examination showed a few epithelial cells and motile bacilli.

Stools: Well formed, pale yellow, waxy, no gross blood, occult blood 0, mucus 0, ova 0. Fat constituent, 29 9 per cent. Maximum normal in dried feces, 22.5 per cent. (Stitt).

Summary of Case.—A boy eighteen and a half years of age in spite of a good appetite has lost 79 pounds in the last three years. He has passed one or two large stools daily. There has been no discomfort during this period except for a gradually increasing emaciation and weakness. Clinically he shows a striking absence of fat in the visible and palpable regions of the body (Fig. 405). There is no evidence of muscular atrophy; no fibrillary twitch

ings, no neurologic changes, no evidence of chronic infection; temperature, pulse, blood-pressure, and basal metabolism are all subnormal, and yet the weight has been steadily decreasing The stools show a fat content of approximately 30 per cent on an average well-balanced diet Unlike Blumgart's cases, he has a normal gastric acidity and very little anemia However, it is probable that this patient has not yet reached the extreme stage presented by Blumgart's case.

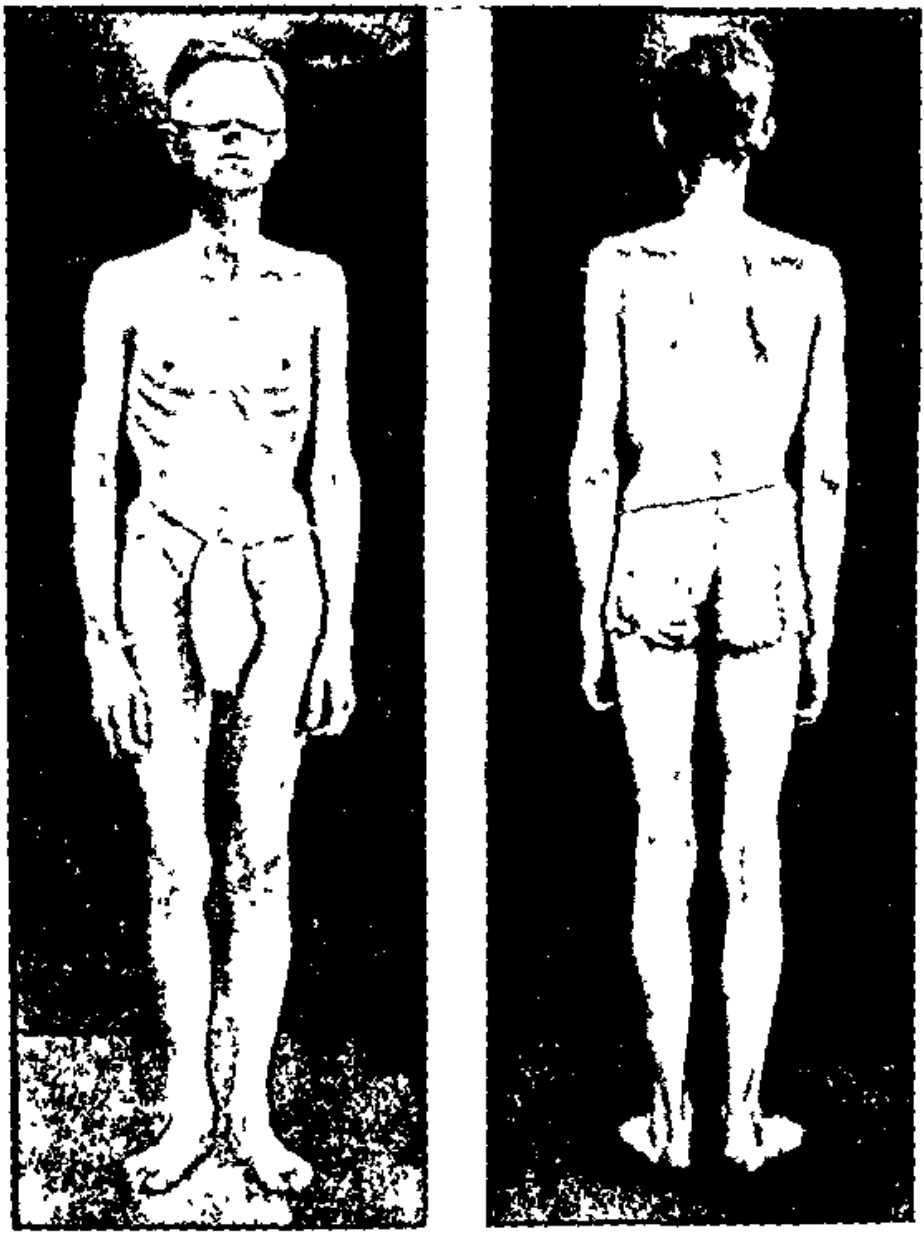

Fig 405.—Photographs of patient with lipodystrophy

Discussion.—Our first impression was that the condition in this case might be due to insufficient intake of food. When we learned, however, that the patient was not constipated and

that he ate fully as much as any other member of his family, it was obvious that the food intake was amply sufficient for his caloric need. The possibility that the condition was due to a chronic infection was ruled out by his history and by the clinical findings, and although the relative increase in the number of blood lymphocytes would suggest the possibility of a chronic infection or even of leukemia, nevertheless it is known that an increase of the number of lymphocytes may occur in any condition of emaciation. The diagnosis of pernicious anemia was not seriously considered; pellagra was ruled out by the absence of dermatitis and polyneuritis; and sprue, in turn, was ruled out by the absence of glossitis, of gaseous diarrhea, and of infestation of the stools. It was obvious, therefore, that we must discover some other source for the disturbed metabolism. Are we dealing merely with malabsorption of fat from the intestinal mucosa, or is this a true lypodystrophy characterized by a profound disturbance of fat metabolism? The former supposition can hardly be considered, since the fat content of the stools, while high, is probably insufficient to account for the loss in weight.

It is true that the necropsy findings of both Whipple and Blumgart appear to indicate that in their cases there was a disturbance in the mechanism of fat absorption through the intestinal mucosa. Nevertheless, it is doubtful whether one is justified in drawing a final conclusion from histologic evidence alone, striking as that evidence may be. Moreover, as for the digestion of fat, in his cases Blumgart was unable to demonstrate any abnormality of the biliary or pancreatic secretion. We know that the fat in food is split up into fatty acids and glycerin by lipase, this process being facilitated by the bile acids, and saponification, in turn, being promoted by the fatty soaps. The fats and glycerin are in part absorbed and are either recombined in the neutral fats in the epithelial tissues or are carried to other deposits by the blood-stream. Thus, approximately 60 per cent. of the fat is carried by the lacteals to the cisterna chyli, while the reamining 40 per cent. goes through the blood.

An important consideration, however, is that the body fat is derived not only from the fat content of the food but also from the carbohydrates; from deaminized amino-acids; from proteins, and from alcohol. It is difficult to believe, therefore, that the fat depots of the body, such as the subcutaneous tissues, the omentum, the mesentery, the retroperitoneal tissues, and the interstitial tissues of the organs could be so strikingly devoid of fat in the presence of a well-balanced diet containing an abundance of carbohydrate and of protein. We know that if the food intake is insufficient for the metabolic needs of the body, fat will be the first substance to be utilized for the supply of energy. We are forced to conclude, therefore, that in such a case as this there is either a malabsorption of all types of food, including fat, or a profound disturbance in fat metabolism

Treatment.—On the basis that we are dealing with a lipodystrophy resulting from a disturbance in the metabolism of fat, the cause of which we have not determined, we have been administering moderate doses of insulin. Since June 16, 1924 the patient has received twice daily a hypodermic injection of 5 units This has been faithfully taken with the exception of three doses until the present time (July 16, 1924). During this month there has been no gain in weight, but a loss of only 1 pound, which is considerably less than his preceding average monthly loss Moreover, the fat content of the stool has been reduced from 29 9 to 26 4 In addition to this the energy and endurance of the patient seem to have increased. Whether this improvement is only subjective or is actual remains to be seen. So far we have not been able to convince this patient that hospitalization is essential for the better study of his condition, but we hope to obtain this end in the near future.

SUMMARY

1. The histologic and clinical evidence revealed in this case appears to us sufficient to consider it as a fifth reported case of progressive or so-called intestinal lipodystrophy.

2. Moderate doses of insulin are being used in the hope of increasing the storage of fat and improving metabolism.

3. The history of previously reported cases has been that of a progressive loss in weight and strength to a fatal termination. The outcome of this case remains to be determined.

REFERENCES

1. Whipple, G. H.: Bull. Johns Hopkins Hosp., 1907, 18, 382.
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